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**Protecting Injecting Drug Users against Blood-Borne  
Viruses: *Modelling the impact of prison-based  
interventions***

by

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A thesis submitted in partial fulfilment of the requirements for the degree of Doctor  
of Philosophy in Biological Science

University of Warwick, Department of Biological Sciences  
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## DECLARATION

The work presented in this thesis is the result of original research carried out by the author, Andrew Sutton. No part of this thesis has been submitted for a degree elsewhere.

### Supervision

The research was carried out under the supervision of Professor Graham F. Medley at the University of Warwick, Dr W. John Edmunds, Mr Nigel J. Gay, and Professor O. Noel Gill at the Health Protection Agency, Colindale, London.

### Publications

Publications arising from this thesis or from work related to this thesis are included in Appendix I. Where work included in this thesis has been published in joint names, the role of each author is outlined below.

#### *Chapter 2*

**Sutton A.J.**, Gay N.J., Edmunds W.J., Andrews N.J., Hope V.D., & Gill O.N. (2005). Modelling the Characteristics of the Male Injecting Drug User Population in England and Wales. *International Journal of Drug Policy* **16**, 176-182

*A.J Sutton was the primary author, constructed the model and analysed the results. N.J. Gay and W.J. Edmunds provided advice and supervised the work. N.J. Andrews provided statistical advice. V.D. Hope and O.N. Gill supplied the data and provided further advice*

#### *Chapter 3 and Chapter 4*

**Sutton A.J.**, Gay N.J., Edmunds W.J., Andrews N.J., Hope V.D., Gilbert R.L., Piper, M., & Gill O.N. (2006). Modelling the hepatitis B vaccination programme in prisons. *Epidemiol Infect.* **134**, 231-242.

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#### *Chapter 5*

**Sutton A.J.,** Gay N.J., Edmunds W.J., Hope V.D., Gill O.N., & Hickman M. (2006). Modelling the force of infection for hepatitis B and hepatitis C in injecting drug users in England and Wales. *BMC Infect.Dis.* **6**, 93.

*A.J. Sutton was the primary author, constructed the model and analysed the results. N.J. Gay and W.J. Edmunds provided advice and supervised the work. V.D. Hope supplied the data. O.N. Gill and M. Hickman helped in the revision of the manuscript and provided additional advice.*

#### *Chapter 6*

**Sutton A.J.,** Gay N.J., & Edmunds W.J. (2006). Modelling the impact of prison vaccination on hepatitis B transmission within the injecting drug user population of England and Wales. *Vaccine* **24**, 2377-2386.

*A.J. Sutton was the primary author, constructed the model and analysed the results. N.J. Gay and W.J. Edmunds provided advice and supervised the work.*

#### *Chapter 7*

**Sutton A.J.,** Edmunds W.J., & Gil, O.N. (2006). Estimating the cost-effectiveness of detecting cases of chronic hepatitis C infection on reception into prison. *BMC Public Health* **6**, 170.

*A.J. Sutton was the primary author, constructed the model and analysed the results. W.J. Edmunds provided advice and supervised the work. O.N. Gill helped in the revision of the manuscript and provided additional advice.*

## **ABSTRACT**

Injecting drug use is a key risk factor, and injecting drug users (IDUs) are a core group for several blood-borne viruses (BBV) including hepatitis B (HBV) and hepatitis C (HCV). In 2003 the Unlinked Anonymous Prevalence Monitoring Programme reported that 62% of surveyed IDUs in England and Wales were found to ever having been imprisoned. Thus prison may provide a good opportunity to administer health interventions against BBVs to this hard to reach population.

The aim of the thesis is to examine a number of alternative intervention measures that target IDUs in a prison setting against BBVs. Methods to inform as to the characteristics of the IDU population and its risk of infection from BBVs are also proposed.

A method to determine the age specific rates at which individuals enter and leave the IDU population is presented. An age-specific dynamic model is developed that describes the flow of IDUs and non-IDUs through prison. This model is used to assess the potential impact of the HBV vaccination programme in England and Wales on the vaccination coverage of the IDU population showing that over 70% of IDUs may be captured with vaccination. Taking data that describes the prevalence of HBV and HCV in current IDUs in England and Wales, the injecting career length specific forces of infection for HBV and HCV in the IDU population in England and Wales are estimated, these provide further evidence that new initiates to injecting may be at increased risk of infection compared to more experienced IDUs. Parameterised models are used to assess the impact that prison vaccination will have on HBV transmission within the IDU population with results showing that prison vaccination may result in a 75% reduction in acute infections in IDUs within 12 years from the start of the programme. Finally the cost effectiveness of HCV case-finding on prison reception is investigated showing the importance of encouraging current or former IDUs to accept ELISA testing on prison reception.

The results provide further evidence that prison may be a good location in which to implement intervention measures against BBVs. The results also provide an increased understanding of the characteristics of IDU population in England and Wales and in particular its risk of infection from HBV and HCV.



## **ABBREVIATIONS AND ACRONYMS**

<b>AIDS</b>	<b>Acquired Immune Deficiency Syndrome</b>
<b>Anti-HBc</b>	<b>Hepatitis B core antigen</b>
<b>Anti-HBc IgM</b>	<b>IgM antibodies to the hepatitis B core antigen</b>
<b>Anti-HBe</b>	<b>Antibodies to the hepatitis B e antigen</b>
<b>Anti-HBsAg</b>	<b>Antibodies to the hepatitis B surface antigen</b>
<b>Anti-HCV</b>	<b>Antibodies to hepatitis C</b>
<b>Anti-HIV</b>	<b>Antibodies to human immunodeficiency virus</b>
<b>BBV</b>	<b>Blood-borne virus</b>
<b>CDSC</b>	<b>Communicable Disease Surveillance Centre</b>
<b>CI</b>	<b>Confidence interval</b>
<b>CRDHB</b>	<b>Centre for Research on Drugs and Health Behaviour</b>
<b>ELISA</b>	<b>Enzyme linked immunosorbent assay</b>
<b>FOI</b>	<b>Force of infection</b>
<b>HAV</b>	<b>Hepatitis A virus</b>
<b>HBeAg</b>	<b>Hepatitis B e antigen</b>
<b>HBsAg</b>	<b>Hepatitis B surface antigen</b>
<b>HBV</b>	<b>Hepatitis B virus</b>
<b>HCC</b>	<b>Hepatocellular carcinoma</b>
<b>HCV</b>	<b>Hepatitis C virus</b>
<b>HCV-RNA</b>	<b>Hepatitis C ribonucleic acid</b>
<b>HIV</b>	<b>Human immunodeficiency virus</b>
<b>HPA</b>	<b>Health Protection Agency</b>
<b>Non-IDU</b>	<b>Non-injecting drug user</b>
<b>PCR</b>	<b>Polymerase chain reaction</b>
<b>RR</b>	<b>Relative risk</b>
<b>SARS</b>	<b>Severe acute respiratory syndrome</b>
<b>UA</b>	<b>Unlinked anonymous</b>
<b>UAPMP</b>	<b>Unlinked anonymous prevalence monitoring programme</b>
<b>WAIFM</b>	<b>‘Who acquires infection from whom’ matrix</b>
<b>WHO</b>	<b>World Health Organisation</b>

## **CHAPTER 1 - INTRODUCTION AND BACKGROUND**

The thesis has two main aims. Firstly, to model the characteristics of the IDU population in England and Wales and in particular consider its risk of infection from HBV and HCV. Secondly to model the impact of a selection of intervention measures on reception into prison including vaccination and case-finding that target IDUs and BBVs.

Background information specifically associated with the IDU population, BBVs and the prison population are presented in this Chapter. In Chapter 2 the characteristics of the IDU population are examined, considering in particular the rates that IDUs start injecting illicit drugs and leave the IDU population. Also considered is the trend in the incidence of injecting drug use and how this may have evolved over time. The findings of this chapter are of importance as they contribute towards the parameterisation of a model of the flow of IDUs through prisons in England and Wales which is the subject of Chapter 3. Chapter 3 is of crucial importance as a model that describes the flow of IDUs through prisons can be applied to investigate many alternative prison based interventions that target IDUs in a prison setting. Using the model of the flow of IDUs through prisons, Chapter 4 considers the effectiveness of the HBV vaccination programme looking particularly at what proportion of the IDU population that may be captured with vaccination. In Chapter 5 the forces of infection (FOI) (the per capita rate at which susceptibles acquire infection) are estimated for HBV and HCV including variation over time and injecting career length. Unlinked anonymous (UA) data on the prevalence of HBV and HCV within the IDU population in England and Wales is fitted to a model by maximum likelihood, with the individual heterogeneity of risk behaviour within the IDU population also being examined. In Chapter 6 the impact of HBV vaccination on prison reception on the transmission of HBV in the IDU population in England and Wales is considered. This chapter uses results from Chapter 4 that describe what proportion of the IDU population is captured by prison vaccination over time, and FOI estimates from Chapter 5. The basis of this chapter is a dynamic mathematical model describing the natural history of HBV to estimate the impact of vaccination on

the prevalence and incidence of HBV within the IDU population in England and Wales. In Chapter 7 the cost effectiveness of a proposed HCV case-finding programme on reception into prisons in England and Wales is examined. Using the model of the flow of IDUs through prison described in Chapter 3 and the HCV FOI estimates in IDUs obtained in Chapter 5, this chapter considers the cost per new chronic HCV case detected on prison reception under a range of screening scenarios while extensive sensitivity analysis is undertaken. Finally, Chapter 8 is divided into two sections. Firstly, the main findings of the thesis are summarised, and then a discussion of the limitations of the studies and potential future work is undertaken.

## 1.1 Injecting Drug Users

Due to their behaviour IDUs are at increased risk of incarceration when compared to non injectors (section 1.4). This may be due to criminal behaviour associated with trying to fund their illegal injecting or in some cases a criminal behaviour may itself have led to an injecting career. The injection of illicit drugs brings its own problems and if injectors share their injecting paraphernalia, as is often the case, then this leads to increased risk from BBVs (section 1.3.1).

The IDU population is a hard to reach population i.e. relatively little is known both about the characteristics and dynamics of the IDU population, and is a difficult population to target for intervention measures that may interrupt the transmission of BBVs. Since IDUs are more likely to go to prison than non-injecting drug users (non-IDUs), this setting may provide a good location in which to target IDUs for intervention measures (World Health Organisation, 2005; Weinbaum *et al.*, 2005).

A particular problem with studying IDUs is the selection of individuals into an analysis. While considering an IDU as being any individual that had used a syringe for taking drugs at least once in his/her life at the start of a survey (Broers *et al.*, 1998) may seem attractive for increasing the number of subjects in the analysis, this definition may include individuals who have long since left their drug using days behind them. Whereas including IDUs that have injected in the four weeks prior to being included in the survey may leave out those IDUs that inject less frequently. In this thesis it has been assumed that a current IDU is defined as a person that has injected in the previous 4 weeks. This was done for two reasons. First, many data sources used throughout this thesis collect data on IDUs that have injected in the 4 weeks prior to having been surveyed. Second, IDUs that inject at least every four weeks are likely to be at greater risk from BBVs and other infections compared to injectors that inject less frequently (section 1.3.1). The success of intervention measures should therefore be judged on the impact they have on these high-risk IDUs.

### 1.1.1 The size and characteristics of the IDU population

Various mathematical and statistical approaches have been made to gain information about the IDU population and its size (Frischer *et al.*, 2001; Godfrey *et al.*, 2002). Large surveys have also been undertaken (Frischer *et al.*, 2001; Johnson *et al.*, 2001; Johnson *et al.*, 1994) with the results extrapolated to draw conclusions about the wider drug using population (Johnson *et al.*, 2001). Many smaller surveys have also been undertaken, but frequently the size of these surveys limits the generalisability of the results between different populations and through time.

It has been suggested that the IDU population in England and Wales has increased substantially in size since the 1980s. Using data on the number of deaths due to opiate overdose it has been estimated that the prevalence of opiate users / injecting drug users has increased from less than 20,000 in 1980 to between 100,000 and 150,000 in 2000 in England and Wales (de Angelis *et al.*, 2004). However this work does assume that opiate overdose deaths have been recorded over the period of the analysis in a consistent manner. Alternative estimates of the prevalence of problematic drug use in the UK undertaken in 2001 have ranged from 161,000-266,000 (Frischer *et al.*, 2001). The proportion of males that have ever injected in Britain has been estimated to be 2.0% in 2000, rising from 1.0% in 1990 (Johnson *et al.*, 2001) however this result must be approached with caution as the persons in the survey were selected from the small-user postcode address file for Britain, and as many current IDUs may be homeless a postcode is something that current IDUs are less likely to have compared to the general population.

The incidence of new initiates to injecting that join the IDU population and how this varies over time is difficult to evaluate due to the delay that occurs from the time of injecting initiation until injectors report to services and can be surveyed. Using back-calculation the incidence of opiate use / injecting drug use in England and Wales using data on the number of opiate overdose deaths by year has been estimated (de Angelis *et al.*, 2004). The authors suggest that the trend in the incidence of opiate use / injecting drug use over time has shown a substantial increase in recent years. While

further evidence of the average age of first injection for an IDU suggests that this often occurs before the age of 20 (Goldberg *et al.*, 1998; Hutchinson *et al.*, 2000; Judd *et al.*, 1999; Muga *et al.*, 2000; Crofts & Aitken, 1997).

A number of factors may lead to a cessation of injecting for an IDU. IDUs that are in contact with a drug network of other injectors have been shown to be significantly more likely to persist with their injecting behaviours. Whereas a decrease in addiction practices and unsafe sexual behaviours have been found to have a significant impact on injecting cessation (Bouhnik *et al.*, 2004). The treatment of IDUs and the kind of treatment that they receive can also have an impact on the rates that IDUs cease injecting. The rate that IDUs stop injecting drugs, the cessation rate, has been estimated in a number of studies. Law *et al.*, (2001) assumed a constant yearly cessation rate of 0.05 which would equate to an average injecting career length of 20 years, while Kaplan, (1989) estimated the cessation rate to be substantially higher at approximately 0.12 per year thereby giving a lower injecting career length of 8 years. Pollack, (2001) assumed that the true cessation rate lay somewhere between and adopted a value of 0.09 which gives an injecting career length of approximately 11 years, although in all these cases the variation of the cessation rate with age was not considered. It must be remembered however when considering the rates IDUs leave the IDU population that in many cases these rates are arbitrary and periods of relapse will often occur (Langendam *et al.*, 2000).

It has been shown that the mortality rate is higher in the IDU population compared to the general population (Ghodse *et al.*, 1998; Sorensen *et al.*, 2005) with estimates of the mortality rate among IDUs ranging from 0.54% (Frischer *et al.*, 1993) to 19/1000 person years (Ghodse *et al.*, 1998). Within the IDU population it has been found that mortality is higher in older IDUs compared to the young (Sorensen *et al.*, 2005), which may be due to riskier injecting practices but may also be due to infection from BBVs such as HBV, HCV, or human immunodeficiency virus (HIV) (section 1.3.1).

## **1.2 Unlinked anonymous prevalence monitoring programme**

The most useful and 'representative' data from which inferences about transmission trends within an IDU population can be drawn, are probably those provided by large voluntary, UA cross-sectional surveys of injectors recruited concurrently from drug services and community sites (Hope *et al.*, 2001).

Since 1990, voluntary UA oral fluid samples have been collected from IDUs in contact with specialist drug agencies throughout England and Wales (Noone *et al.*, 1993; Nicoll *et al.*, 2000). These agencies provide services including needle exchange, methadone maintenance and outreach work. Behavioral information is collected through a brief anonymous questionnaire unlinked from client identifying information. This includes questions on previous HIV testing, characteristics of the IDU population, and the sharing of injecting equipment. Fluid samples can inform as to the prevalence of BBVs in the IDU population including HBV, HCV and HIV (section 1.3.1). These samples have been collected on an annual basis leading to the availability of 15 complete surveys (1990-2004), although they do not extend to Scotland or Northern Ireland where other methods of surveillance are used (Health Protection Agency *et al.*, 2005). As data from these surveys is used regularly throughout this thesis they are referred to as the UAPMP surveys from here on.

While it is acknowledged that data such as this is representative of IDUs that are in contact with services (Hope *et al.*, 2002), the IDUs recruited into the survey are self-selected and may not be representative of the whole IDU population. Surveys of injectors that are in contact with services will inevitably lead to some bias, IDUs that have short careers will be under sampled whereas older injectors will be over represented and this can lead to a bias in the conclusions drawn from the data. Comparisons have been made between IDUs both in and out of drug treatment. IDUs that report to services are generally older (Cook *et al.*, 2001) and have a longer average injecting careers than those that do not (Godfrey *et al.*, 2002). Work has also been done to estimate the lag from the time of heroin use initiation until the time of first reporting (Hickman *et al.*, 2001). It has been speculated that the average delay

from the time a person starts problematic drug use to receiving treatment is 5 years (Coid *et al.*, 2000; Godfrey *et al.*, 2002) or more. These caveats must all be remembered when drawing conclusions from UAPMP survey data.

### **1.3 Injecting drug users and their risk from infection**

#### **1.3.1 Blood-borne viruses**

A BBV is transmitted when blood from an infected person gets into the bloodstream of another (Health Protection Agency, 2006). It has been shown that IDUs are at increased risk from BBVs due to risky behaviour associated with their injecting behaviour (Hahne *et al.*, 2004; Patrick *et al.*, 2001; Rhodes *et al.*, 1996). Risk factors within the IDU population that have been identified as leading to increased prevalence and incidence of BBV infection include the sharing of needles and injecting paraphernalia, frequency of injection, repeated injecting with used needles, or the inadequate cleaning of injecting paraphernalia (Patrick *et al.*, 2001). In the case of those BBVs that can also be transmitted via sexual contact, this can assist in the transmission of BBVs between IDUs and non-injecting populations. It is not unusual to find that IDUs with a specific ethnicity to be at greater risk from BBVs compared to the general IDU population. This was seen in IDUs with African-American ethnicity in a study of IDUs recruited through street outreach in Baltimore, Maryland in 1988-1989 (Levine *et al.*, 1995). This is likely to be due to increased sharing behaviour and perhaps increased prevalence within specific ethnic groups.

While it is often not possible to prove conclusively that observed BBV infections over time are due to the sharing of injecting equipment, it is likely that most acquired their infection this way (Roy *et al.*, 2001). In many cases injecting drug use will be the only risk factor in those injectors that are found to be infected from BBVs. The attendance of 'shooting galleries', places where drug injection equipment is sequentially rented to users resulting in some users injecting with previously used equipment (Kaplan, 1989) is also highly correlated with BBV incidence and prevalence (Patrick *et al.*, 2001). Providing further evidence of the risk that used injecting equipment poses to IDUs.



It is common amongst studies of the IDU population to find the prevalence of BBVs being associated with injecting career length, with those IDUs with longer injecting careers more likely to have evidence of past BBV infection compared to new initiates to injecting. This can also be said of older injectors compared to younger injectors although injecting career length and age are often found to be highly correlated (Rhodes *et al.*, 1996). However the incidence of BBVs is often found to be higher amongst new initiates to injecting (van Beek *et al.*, 1998). This is due to new initiates being more likely to share injecting paraphernalia in the early days of their injecting career before their injecting practices have been established (Rhodes *et al.*, 1996). In the case of HCV in England and Wales (section 1.3.1.2) evidence has shown that HCV infection in IDUs is difficult to prevent and that infection is acquired rapidly after initiation into injecting (Hope *et al.*, 2001). It has been suggested that younger IDUs could be at relatively higher risk of infection compared with uninfected older IDUs if being uninfected becomes a marker of well-established prevention practices with increasing duration of injection and age. Thus, increasingly lower risk cohorts of IDUs may be established with increasing age as those at higher risk are removed because of BBV seroconversions (van Beek *et al.*, 1998).

A major issue with BBVs is that many carriers may be unaware of their infection (Rhodes *et al.*, 1996), particularly if there are no symptoms following infection as can be the case with HBV, HCV, and HIV. IDUs that are unaware of their infection can unknowingly contribute to transmission between the IDU population and non-IDU populations if the infection is transmissible via sexual contact. It has been found in the UAPMP surveys (Health Protection Agency *et al.*, 2005) that 49% of IDUs self reported that they were unaware of their HCV infection while an alternative study (Schlichting *et al.*, 2003) found that in IDUs that tested positive for HCV only 23% of them were aware of their positive status. This lack of awareness of their infection status imposes a considerable barrier to transmission prevention.

#### **1.3.1.1 Hepatitis B**

HBV is transmitted by parenteral exposure to infected blood or body fluids, with transmission most frequently occurring either through sexual intercourse, as a result of blood-to-blood contact typically through the sharing of needles and other equipment by IDUs, or through perinatal transmission from mother to child. Transmission can also occur through transfusion-associated infection, although this is now rare in the UK as all blood donations are screened (Salisbury & Begg, 1996).

It is estimated that 0.3% of the UK population is chronically infected with HBV which is equivalent to approximately 180,000 people. In 2003 there were approximately 1,300 cases of acute HBV in England and Wales reported to the Health Protection Agency (HPA) with the most common reported risk factor being injecting drug use (Health Protection Agency, 2006). The incidence of infection in the general population of England and Wales has been estimated at 7.4 per 100,000 although this does not represent the huge heterogeneity of risk within the population with high risk groups being determined mainly by country of birth, ethnicity, and adult risk behaviours such as injecting drug use (Hahne *et al.*, 2004).

The average incubation period ranges from 40-160 days. Current infection can be detected by the presence of HBV surface antigen (HBsAg) in the serum. The risk of developing chronic HBV infection is heavily age dependent and is defined as persistence of HBsAg in the serum for six months or longer (occurring in 2-10% of those infected as adults rising to approximately 90% in those infected perinatally). Among carriers of the virus, those in whom HBV e-antigen (HBeAg) is detected are most infectious. Those with antibody to HBeAg (anti-HBe) are generally of low infectivity. This is summarized in Table 1.1.

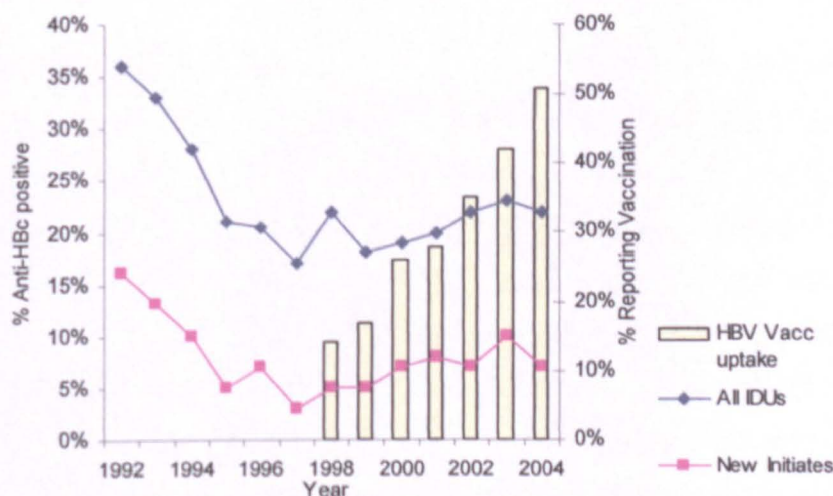
**Table 1.1 - Hepatitis B: diagnosis**

Status	Detection of					
	Anti-HBc	Anti-HBc IgM	HBsAg	Anti-HBs	HBeAg	Anti-HBe
Acute (infectious)	+	+	+	-	+/-	+/-
Carrier (low infectivity)	+	-	+	-	-	+
Carrier (high infectivity)	+	-	+	-	+	-
Recovery (immune)	+	-	-	+	-	+/-
Immunity (after vaccination)	-	-	-	+	-	-

Safe and effective vaccines to prevent HBV infection have been available since 1992, with the World Health Organisation (WHO) having recommended that all countries adopt universal HBV vaccination by 1997. This has not been adopted in England and Wales where instead a policy of selectively immunizing key at risk groups from HBV infection has been implemented. This approach to vaccination in England and Wales has been justified by the low incidence of HBV infection within the general population (Hahne *et al.*, 2004). A course of HBV vaccinations consists of three doses of vaccine with a booster dose typically administered 12 months after the 1<sup>st</sup> dose. The timing of the first three doses is variable and is usually implemented at zero, one, and six months. For high risk groups faster schedules are implemented with an accelerated schedule being 0, 1, and 2 months and a super accelerated schedule being 0, 7 and 21 days although the super-accelerated schedule is not licensed for those under 18 years of age. The improved compliance of these faster schedules is likely to offset any reduced immunogenicity when compared to the 0, 1, and 6 months schedule (Christensen *et al.*, 2004; Bock *et al.*, 1995).

The IDU population in England and Wales is the largest at-risk group from HBV infection. Data from the UAPMP surveys in 2003 suggested that amongst those cases of acute HBV with an identified risk factor, 34% were attributable to injecting drug use. The proportion of IDUs in England and Wales ever infected by HBV (anti-HBc positive) in 2004 was approximately 22% (Health Protection Agency *et al.*, 2005). The trend over time has shown a decrease overall since 1992 although since 1999 a slight increase has been noted. Amongst new initiates to injecting (defined as IDUs that started injecting in the three years prior to participating in the survey) similar trends are seen (Figure 1.1). HBV vaccine uptake (receiving one or more vaccine doses) in the IDU population has shown a steady increase since 1998 up to over 50% in 2004 (Health Protection Agency *et al.*, 2004) although the location of vaccination is not reported. However the overall HBV vaccination coverage in the IDU population is likely to be lower as many IDUs are not in contact with drug agencies.

Figure 1.1 - Trends in the HBV vaccine uptake and past HBV infection amongst IDUs in England and Wales (Health Protection Agency *et al.*, 2005).



Where all IDUs are defined as having injected in the previous 4 weeks and new initiates to injecting started injecting drugs in the previous three years

### **1.3.1.2 Hepatitis C**

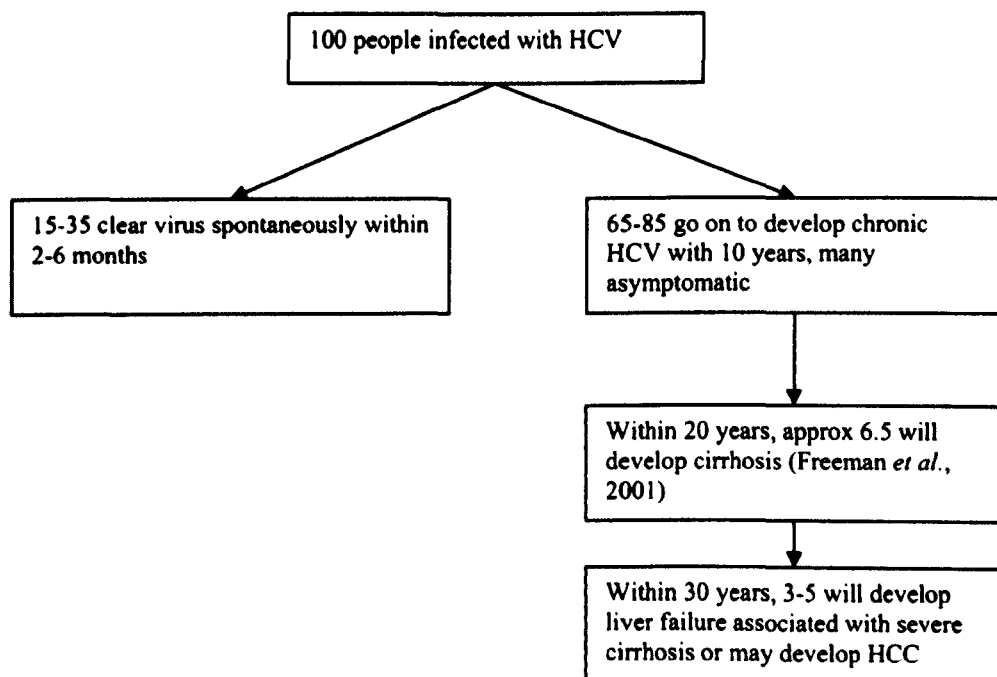
The WHO estimates that some 170 million people are chronically infected with HCV (World Health Organisation, 1999). On a global scale, the United Kingdom is considered to be a relatively low prevalence country. In 2002, the HPA estimated that the prevalence of HCV-specific antibodies (anti-HCV) in the general population is approximately 0.5%. While it has been estimated that there are approximately 200,000 individuals chronically infected with HCV in England (Health Protection Agency Centre for Infections, 2005).

The transmission of HCV predominantly occurs through blood-borne transmission such as injecting drug use and blood-transfusion although transmission can occur via routes such as mother to baby and sexual exposure although these are less efficient (Balogun *et al.*, 2002). As with HBV the transmission of HCV due to blood-transfusion in England and Wales is rare due to the screening of all blood-donations.

There are six major HCV genotypes (1 to 6) with a variety of subtypes existing within each genotype. In the UK genotype 1 is the most common found in 40-50% of cases, genotypes 2 and 3 contribute another 40-50% while genotypes 4, 5, and 6 constitute the remainder of about 5%. The genotype of the virus has been found to be the most important determinant of efficacy of treatment. Combination therapy with pegylated interferon alfa and ribavirin is recommended for the treatment of people aged 18 years and over with mild to severe chronic HCV. Overall, this treatment is successful in clearing the infection (leaving no detectable virus in the blood 6 months after treatment has ceased) in up to 55% of patients. The effectiveness of treatment varies according to the infecting genotype, from 45% in those infected with genotype 1, up to 80% in those infected with genotypes 2 and 3. However, not everybody is suitable for treatment or can tolerate it. Factors such as age, sex, duration of infection, the strain of the virus, and the degree of existing liver damage determine the effectiveness of treatment (National Institute for Clinical Excellence Guidelines, 2004).

After HCV infection hepatitis C ribonucleic acid (HCV-RNA) can be detected in 1-3 weeks with the acute phase lasting 2-3 months. Of those infected 65-85% will develop chronic HCV and approximately 6.5% will develop cirrhosis within 20 years (Freeman *et al.*, 2001). Within 30 years 3-5% of those infected will develop liver failure associated with severe cirrhosis or may develop hepatocellular carcinoma (HCC). In many cases the infection will not be apparent for many years this is partly because the liver has the capacity to 'cope' with the infection. Symptoms do not often develop until the liver has been quite extensively damaged. Alcohol consumption, acquiring the infection at an older age, and being male, have all been shown to be associated with more progressive disease (Stein *et al.*, 2002). The natural progress of HCV is summarised in Figure 1.2.

Figure 1.2 - Example of the natural progression of 100 people infected with HCV.

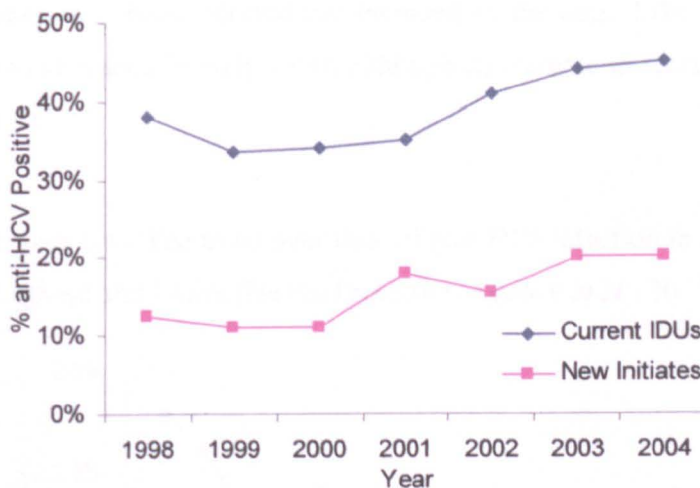


(Stein *et al.*, 2002)

In England and Wales it has been suggested that HCV is currently the most significant infectious disease affecting those who inject drugs (Health Protection

Agency *et al.*, 2005). Amongst the reported laboratory diagnoses of HCV infection in England in 2004, 95% of those with exposure data were attributable to injecting drug use. UAPMP surveys have reported an increase in current IDUs (injected in the previous 4 weeks) that have antibodies to HCV (anti-HCV) in recent years up to 45% in 2004, while a similar increase has been seen in new initiates to injecting (started injecting within the three years prior to participating in the survey). This is shown in Figure 1.3:

Figure 1.3 - The trend over time of past HCV infection in current IDUs and new initiates to injecting in England and Wales (Health Protection Agency *et al.*, 2005).



Where current IDUs are defined as having injected in the previous 4 weeks and new initiates to injecting started injecting in the past three years

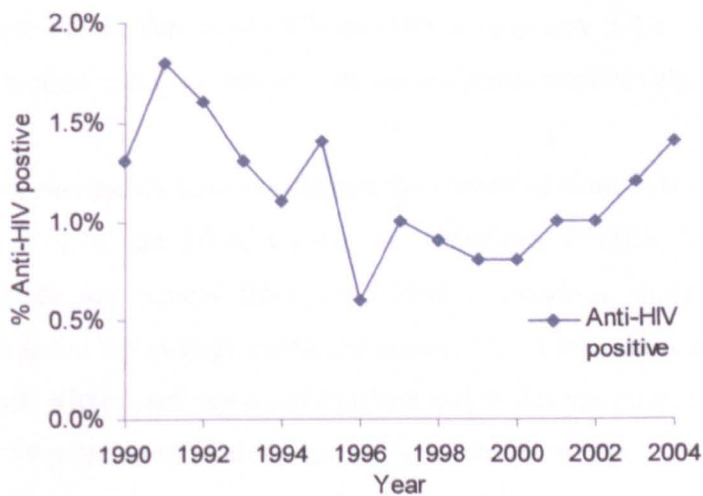
As many HCV infections are asymptomatic, it is of benefit if those individuals that have undiagnosed infection can be identified. Testing for anti-HCV antibody is now widely available, sensitive (>95%) and relatively inexpensive, and case identification may be beneficial to patients, their families and to the general population. For patients that are found to be eligible treatment maybe offered (Gordon, 1999).



### 1.3.1.3 HIV

In 2004 the number of prevalent HIV infections among adults aged 15-59 in the UK was estimated to be 58,300. However, unlike HBV and HCV, injecting drug use is not the biggest risk factor for HIV infection with only an estimated 2,000 cases being due to injecting drug use, the remainder being predominantly due to either sex between men or heterosexual sex. Overall HIV infection among IDUs in the UK remains relatively rare with around one in every 65 injectors infected (Health Protection Agency *et al.*, 2005). UAPMP survey data show that the prevalence of HIV infection is very low compared to HBV and HCV even when individuals that have ever been injected are included in the data. Like HBV, HIV prevalence has shown a drop in early 1990s although an increase in recent years can be seen (Figure 1.4).

Figure 1.4 - The trend over time of past HIV infection in current and former IDUs in England and Wales (Health Protection Agency *et al.*, 2005).



Where current IDUs are defined as having injected in the previous 4 weeks

As the prevalence of HIV is low in the IDU population of England and Wales compared to HBV and HCV it has not been considered in this thesis. However it is acknowledged that a measure of the success of intervention measures that target



IDUs would be to consider their impact on the incidence and prevalence of HIV within the IDU population over time.

#### *1.3.1.4 The incidence of Blood-borne viruses*

As FOI of HBV and HCV will be considered in a later chapter (Chapter 5), a brief review of studies that consider the incidence of HBV, HCV, and HIV in England and Wales is included here.

The incidence of infection is often used to gain some idea as to the FOI of a particular infectious disease where the FOI is defined as the per capita rate at which susceptible individuals acquire infection. Calculation of incidence is sometimes undertaken through the use of cohort studies in which IDUs are classified on the basis of the presence or absence of exposure to a particular factor and then followed for a specified period of time to determine the development of disease in each exposure group (Hennekens & Buring, 1987). This was the case in Judd *et al.*, (2005) where the incidences of HCV and HIV among new IDUs in London were found to be 41.8 cases and 3.4 cases per 100 person years, respectively.

Previous studies have considered the reports of acute HBV in England and Wales as reported to the HPA, Centre for Infections (Health Protection Agency, 2006). Considering reports from 1985-1996 a previous study (Balogun *et al.*, 1999) calculated the average estimated annual rate of laboratory reported HBV infection in adults within each region of England and Wales varied from 1.27 to 2.81 per 100,000 of the population, with the majority of reports being from symptomatic individuals. However this study considered the rate of reported acute HBV infection rather than a true HBV incidence that would include both asymptomatic and symptomatic individuals. Hahne *et al.*, (2004) also considered data reported to the HPA, Centre for Infections of acute HBV infections in England and Wales from, 1<sup>st</sup> January 1995 – 31st December 2000 (Health Protection Agency, 2006). However this study considered the impact of under reporting in the population where some persons infected by HBV for whatever reason would not necessarily report their infection.

Also considered in the incidence calculations was the proportion of infections that are asymptomatic which can also impact on incidence calculations. Taking these factors into account the authors found a higher HBV incidence estimate for England and Wales being 7.4 per 100,000, with injecting drug use being the most frequently reported route of transmission.

An alternative proxy for incidence in the whole IDU population is to consider the prevalence of BBVs in new initiates to injecting as was seen in sections 1.3.1.1 and 1.3.1.2. Assuming that these IDUs have only been exposed to BBVs during their injecting careers and were not at risk before the start of their injecting career then these individuals can provide a useful insight into the trend of recent infection over time within the IDU population. However it must be remembered when using this technique to make conclusions about the FOI in the overall IDU population that it has to be assumed that the at-risk behaviour of new initiates is the same for the rest of the IDU population.

In an attempt to estimate the incidence of BBVs in the IDU population, studies have attempted to follow IDUs over time through the use of prospective cohort studies. However this approach may be biased as those IDUs that are not infected may not be highly street entrenched (i.e., are not involved in a chronic and intractable way with the street scene) and are therefore less likely to return for follow-up visits (Patrick *et al.*, 2001). In addition to this the number of person years injecting, often used to calculate the incidence of BBVs in the IDU population will often be over estimated since information may not be available on periods of injecting abstinence due to, for example, imprisonment, hospitalization or drug treatment (Roy *et al.*, 2001).

### 1.3.2 Other infections

The three main BBVs that occur in the IDU population are HBV, HCV, and HIV have been discussed. However these are not the only infections that IDUs are vulnerable to, and so for completeness a brief review of a selection of other infections is included here.

Hepatitis A (HAV) infection may occur in the IDU population through person-to-person contact with other infected individuals through poor-hygiene, via blood through sharing contaminated injecting equipment, through sexual activities that increase risk of oro-faecal contamination, or from drugs that have been contaminated with faeces during smuggling. An effective vaccination is available. In 2004 the number of laboratory reports of HAV in England and Wales was 627 compared with 984 in 2003 and 1,352 in 2002. Only a small proportion of these reports in 2004 contained information on risk factors with 73% reporting travel abroad as the main risk factor rather than injecting drug use (Health Protection Agency *et al.*, 2005). In the early part of the decade there had been a number of outbreaks of HAV that were associated with IDU and homelessness (Perrett *et al.*, 2003). However 2004 data suggest that the outbreaks of HAV in IDUs have been waning.

IDUs are also vulnerable to a range of bacterial infections as a result of non-sterile injecting or injecting contaminated drugs, a brief summary of which is given below (Health Protection Agency *et al.*, 2005):

*Staphylococcus aureus* is a common pathogen among IDUs, causing infections that vary in severity from minor skin and soft tissue infections through to life-threatening invasive disease such as bacteraemia and endocarditis.

*Group A Streptococci* can cause skin sepsis, bacteraemia and necrotic infections among IDUs through infection of injecting sites.

*Clostridial infections*; clostridia are a group of spore forming bacteria that are widely found in the environment. The spores produced by these bacteria may be found in drugs, such as heroin, through environmental contamination. They may cause wound infections among IDUs, particularly if they enter an intramuscular or subcutaneous

injection site, and can then produce toxins causing illness such as tetanus or 'gas gangrene' with a potentially fatal outcome.

Botulism is an illness caused by botulinum toxin, a poison produced by the bacterium *Clostridium botulinum*. Symptoms of botulism include blurred vision and difficulty in swallowing and speaking and may cause paralysis and death. However there is an effective antitoxin. When it infects wounds, including injecting sites, it causes wound botulism. Up until 2000 there had been no case of wound botulism reported among IDUs in the UK however by 2004 89 cases had been reported suggesting that this may be a growing problem.

Neither HAV nor bacterial infections are given further consideration during this thesis although as with HIV, surveillance of these infections over time may provide a good measure of the success of future intervention measures that target the IDU population.

#### **1.4 Injecting drug users and crime**

Due to criminal behaviour associated with drug use, IDUs are at increased risk of becoming incarcerated compared to the non-drug using population. For example UAPMP surveys reported that 62% of surveyed IDUs in 2003 were found to have been in prison (Health Protection Agency *et al.*, 2005). This is also verified in surveys undertaken in prisons that show the high proportion of prisoners that are found to have injected drugs (Gore *et al.*, 1997; Weild *et al.*, 2000).

It is accepted that illicit drug use and crime are associated and develop together, amongst illegal drug-using criminals the need for drugs may cause crime on a day-to-day basis or both may tend to be determined by some other set of factors. A typical theory suggests that addiction causes crime. During periods of heavy drug use or 'addiction', drug users commit more crimes to finance their expensive habits. This is in comparison to periods of treatment or abstinence when users commit fewer crimes. Although alternatively it has been suggested drug use and crime co-occurs because

the people who become criminals are also likely to become drug abusers (Hammersley *et al.*, 1989).

It has been found that the offending characteristics of IDUs are significantly different when compared to non-IDUs. Due to their behaviour associated with injecting drug use, IDUs are more likely to go to prison than non-IDUs, and there is also evidence of IDUs being given shorter prison sentences than non-IDUs (Bird *et al.*, 1995; Weild *et al.*, 2000). This suggests that the turnover of IDUs through prison is more rapid than non-IDUs as they pass through prison more rapidly and frequently.

An important risk factor for BBV prevalence within the IDU population is a history of previous imprisonment (Patrick *et al.*, 2001; van Beek *et al.*, 1998). During any period of incarceration it has been shown that some IDUs will continue their injecting behaviour (Gore *et al.*, 1995b; Gore & Bird, 1998; Covell *et al.*, 1993; Allwright *et al.*, 2000), and while the prevalence of injection within prisons are probably much less frequent than outside (Hutchinson *et al.*, 2000), those who continue to inject are highly likely to share needles when they are imprisoned, thus facilitating the spread of BBVs (Macalino *et al.*, 2004; Covell *et al.*, 1993). Evidence of a high risk needle sharing environment inside prisons has been seen in many previous studies (Gore *et al.*, 1995b; Gore & Bird, 1998; Boys *et al.*, 2002; Covell *et al.*, 1993), and there is evidence of the rapid spread or outbreaks of BBVs in prisons, this inevitably being due to a high level of circulating virus among inmates who practice needle sharing with ineffective cleaning and a limited number of needles (Taylor *et al.*, 1995; Hutchinson *et al.*, 1998).

Prison also poses an added risk to non-IDUs, it is common to find evidence of injectors that initiated their injecting career during a period of incarceration (Gore *et al.*, 1997; Gore *et al.*, 1995b; Boys *et al.*, 2002; Gore *et al.*, 1995a). It may be inferred from this that there are IDUs that wouldn't otherwise have initiated their injecting career except as a result of a spell in prison. However it has also been suggested that as some injectors discontinue their injecting while in prison, incarceration may have a protective effect on their health. Although the restricted access to drugs and injecting equipment does not prevent many from injecting in

prison for the first time and placing all those who do inject in prison at vastly increased risk of contacting infections (Taylor *et al.*, 1995).

### **1.5 Interventions targeting the IDU population**

It has been shown that IDUs are at increased risk from BBVs and other infections and it is therefore of public health importance if interventions that target this high risk group can be implemented. A number of interventions have been proposed that target individuals within the IDU population; these include vaccination, education, treatment, and needle exchange programmes (Francois *et al.*, 2002).

Where possible individuals at high risk from BBVs should be vaccinated (Salisbury & Begg, 1996). As has already been shown the prevalence of BBVs in the IDU population is much higher than in the general population (section 1.3.1). In the case of HBV, despite WHO recommendations the UK has not implemented a universal vaccination strategy and so in this case individuals at greatest risk particularly IDUs should be targeted for vaccination (Hahne *et al.*, 2004; McGregor *et al.*, 2003). Data from the UAPMP surveys in 2003 (Health Protection Agency *et al.*, 2005) showed that amongst current IDUs that report receiving HBV vaccination a reduced HBV prevalence can be seen (19% infected in the unvaccinated and 14% infected in the vaccinated). While this suggests that some IDUs are being infected prior to receiving vaccination, this does provide evidence that vaccination can impact on HBV transmission within the IDU population. From a previous study using semi-structured interviews with needle exchange staff (McGregor *et al.*, 2003) it was found that the main barriers to vaccine uptake amongst IDUs include difficulties in contact tracing household contacts, IDUs chaotic lifestyles, and, the failure of services such as drug treatment, family doctors, and prison service to start or complete courses. Whereas enablers of vaccine uptake include administering vaccine in a variety of venues and settings, monitoring of vaccine courses, reminders in records to prompt next doses, and accelerated vaccine courses. Factors associated with vaccination may be applicable in settings where there are concerted campaigns to improve vaccine uptake in IDUs.

A needle exchange programme is defined as an organised service for the exchange of sterile needles and syringes used for injections as a potential means of reducing the transmission of infectious diseases (www.biology-online, 2006). Evidence of the impact that needle exchanges can have on the transmission of BBVs was shown from IDUs in New York City, in which the incidence of HIV seroconversions was significantly lower among IDUs who were regular users of a syringe / needle exchanges than among non-users. Further analysis has shown that the mean annual HIV seroprevalence rate for 29 cities with exchange programs had fallen by 5.8%, whereas that for 52 cities without such programmes had increased by 5.9% (Mansson *et al.*, 2000). This finding has been echoed in Glasgow where sizeable reductions in anti-HCV prevalence among, newly initiated, injectors from Glasgow and Lothian from the early to mid 1990s support the hypothesis that harm reduction interventions, particularly needle exchanges may have played an important role in reducing the spread of HCV (Hutchinson *et al.*, 2002).

Knowledge of infection may impact on injecting behaviour and may lead to a reduction in the behaviour that leads to further infection within the IDU population. However this must be tempered against the possibility that identifying a positive individual with a BBV may impact on their quality of life (Forman *et al.*, 2000; Rodger *et al.*, 1999; Tompkins *et al.*, 2005). Lifestyle modifications can be made to decrease the risk of further BBV transmission with education increasing overall public awareness of the disease and potentially improving prevention efforts (Gordon, 1999). In the case of patients that are HCV positive they can be counselled to avoid alcohol consumption and as these individuals typically share the same risk factors that lead to HAV and HBV infection, vaccination against these viruses may also be offered if appropriate (Salisbury & Begg, 1996).

Measuring the impact of interventions that target the IDU population is hampered by the fact that IDUs, owing to the illegal nature of their drug use, are a 'hidden' population. In addition, the introduction of concurrent interventions makes it difficult to attribute positive changes within the population to any one of them. Nevertheless, as has been shown studies evaluating BBV prevalence and incidence rates, as well as

risk-taking behaviour among IDUs, have been published. Most of them show a considerable reduction in risk behaviour after the introduction of prevention activities (such as methadone maintenance programmes and needles exchanges) as well as a decline in the incidence of BBV infection and a stabilization or reduction in BBV prevalence (Broers *et al.*, 1998).

#### 1.5.1 Targeting the injecting drug user population in a prison setting

Due to the illegality of injecting drug use and the close association between crime and drug manufacture, trafficking, supply, and use, those involved with injecting illicit drugs frequently pass through prisons (Skipper *et al.*, 2003). This suggests that prison may be a good location in which to administer intervention measures targeting the IDU population. These intervention measures may include but are not limited to vaccination, rehabilitation and treatment, and the exposure to screening programmes (McGregor *et al.*, 2003). Suggested recommendations that should form the basis for HBV prevention programmes within European prisons have included HBV vaccination for all inmates upon entry into prisons, the introduction of accelerated immunisation schedules with the aim of achieving higher vaccine uptake levels among prisoners, and being permitted access to drug rehabilitation programmes for inmates that inject drugs (Francois *et al.*, 2002).

In April 1999, the Scottish Prison Service implemented an initiative to offer HBV vaccination to all inmates. With the high rate of imprisonment (for short stays) among IDUs (section 1.4), it was concluded that any appreciable impact of this initiative should be evident in community-based IDU populations soon after its implementation. Four voluntary, anonymous cross-sectional surveys of Glasgow's IDUs were conducted in 1993, 1994, 1999 and 2001-2002. From these surveys it was observed that vaccine uptake increased significantly in all groups according to recruitment setting, gender, age, time since onset of injecting, having received treatment and imprisonment. But a much smaller rise in uptake was also observed among IDUs who had not been imprisoned since the onset of injecting. Observations in Glasgow showed that the uptake of at least one dose of HBV vaccine had more



than tripled (16% to 52%) among recent initiates to injecting drug use (i.e. those who had commenced injecting within the previous five years) in the two years since the introduction of universal HBV vaccination in prisons and young offender institutions. Since the introduction of vaccination in Scotland, no outbreaks of HBV among IDUs that had been witnessed prior to the introduction of vaccination have occurred (Hutchinson *et al.*, 2004). Further evidence of the impact of HBV vaccination in prison settings has been seen in the low prevalence of HBV found in prisoners in the Republic of Ireland (Allwright *et al.*, 2000) where there is a policy to offer vaccination to all prisoners with sentences of eight months or longer.

As has already been discussed it is of advantage to identify those individuals that may have undiagnosed BBV infection (section 1.5), and that this may be undertaken in a prison setting. A previous study (Horne *et al.*, 2004) has suggested that offering case-finding to all prisoners is less effective than screening in specialist treatment services although this conclusion is largely based on the small numbers of eligible individuals that accepted HCV treatment. However the authors do argue that it may be possible to improve the effectiveness of HCV screening in the prison setting, with recommendations that include developing a standard HCV screening pathway across all prisons and focusing efforts to improve screening uptake among IDUs. An alternative study (Allen *et al.*, 2003) argues that with its closely monitored environment, prison can provide a unique opportunity to identify and treat patients with HCV in a secure setting that may be a safer environment than other community settings. Additionally as most patients treated for HCV have drug dependence histories, prisons can provide an opportunity to treat during a period of forced sobriety.

In many countries community drug treatment services have evolved considerably over the past decade with needle exchange and methadone maintenance becoming widely available (Allwright *et al.*, 2000). However health care in prison settings often have not kept pace with these changes meaning that many IDUs that receive treatment for their drug abuse outside prison do not continue their treatment inside prison (Gore & Bird, 1998). An example of this is the case of the Irish prison healthcare system which has not kept pace with the treatment services available in

the community (Allwright *et al.*, 2000). Evidence suggests that there is a need to consider increased provision of measures to reduce harm in Irish prisons and elsewhere.

With evidence of their increased risk of infection (section 1.3.1) new initiates to injecting are ideal candidates to be targeted in an attempt to reduce the transmission of infection within IDU populations. The IDU population is a hard to reach population for intervention measures with new initiates in particular being hard to access, as is evidenced in the reduced number of new initiates to injecting that appear in the UAPMP surveys in England and Wales (Health Protection Agency *et al.*, 2005). However new initiates to injecting can still be imprisoned and prison may therefore provide a good location in which to capture this otherwise hard to reach population with drug related interventions.

#### *1.5.1.1 Hepatitis B vaccination programme in England and Wales*

The following description of the HBV vaccination programme in England and Wales has made use of a previous study (Gilbert *et al.*, 2004).

A vaccination programme offering HBV vaccine at reception into prison began in England and Wales in June 2001. During 2002 it was estimated that approximately 5% of all prisoners on reception into prisons in England and Wales were offered at least 1 dose of HBV vaccine, rising to approximately 15% in 2005.

Prisoners are eligible for vaccination on each reception into prisons that are participating in the vaccination programme. The current prison policy in England and Wales for adults is to use the super-accelerated programme with injections at 0, 7, and 21 days and a booster at the 12-month stage. This programme is not licensed for juveniles (<18 years), and so in their case an accelerated programme is administered at 0, 1, and 2 months with a booster again at the 12-month stage. A person who stays in prison for less than the time it takes to administer 3 doses will not complete the vaccination programme.

Ensuring that prisoners complete the full course of injections before they leave prison is an on-going problem particularly when prisoners may be imprisoned for less than 21 days. A further barrier to vaccination uptake within prisons is that prisoners are frequently moved between establishments often at short notice with vaccination being discontinued if the new prison is not participating in the programme. However over time, persistent offenders will begin returning to prison having already received vaccination in prison. As the recidivism rate is particularly high among IDUs this would indicate that this population group may be vaccinated effectively (receive a complete dose of vaccinations) over a series of custodial sentences rather than just one sentence. As more persons return to prison that have been previously vaccinated, less doses of vaccine will be required to maintain vaccination coverage.

It has been found in prisons that are less efficient at delivering vaccination that valuable time is often lost between the prisoner being informed about the vaccination programme on reception and the first dose of vaccine being given. The logistical problems of locating prisoners and subsequently moving them to relevant treatment rooms are often blamed. However, several prisons have overcome this by introducing wing-based clinics situated closer to the prisoners. Problems are also associated with vaccinating prisoners who were reluctant to miss activities such as work, for which they are paid, and legal and domestic visits. Although funding is available for additional staff, prison healthcare centres frequently suffer understaffing issues because of recruitment and staff retention problems.

## **1.6 Modelling the IDU population**

### **1.6.1 Injecting and sharing**

It has been shown that within the IDU population transmission of BBVs are most likely to occur when injectors share their needles and injecting paraphernalia with other injectors (section 1.3). Therefore models of the IDU population that describe the transmission of infections with emphasis on injecting and sharing practices are of

particular interest. The literature under review was identified through manual and computerised searches of the Pubmed and ScienceDirect databases using the subject headings of “modelling” and either “injecting” or “IDU”. Additional papers were obtained by considering references in the papers as they were identified. Papers published from 1989-2006 were identified.

In the past numerous intervention programmes have been carried out within various IDU populations around the world; these have included outreach education programmes, testing, counselling, bleach distribution, and access to clean needles and needle exchange programmes (section 1.5). However the impact of these and other prevention strategies can be difficult to measure due to the challenges of follow-up and confounding. Mathematical modelling can be used as an alternative means to overcome some of these problems.

Murray *et al.*, (2003) propose a simple deterministic model that describes the injecting behaviour of IDUs. Using this model it is possible to evaluate the effect on the prevalence and incidence of HCV and HIV within the IDU population of those intervention measures that target a change in the injecting behaviour of IDUs. Typical intervention measures that can be examined include reduction in the frequency of injections, the cleaning of needles or a reduction of IDUs taking part in each injection event. However this model has a number of shortcomings, it relies heavily on the estimated size of the IDU across the years of interest as an input into the model, and is extremely sensitive to model parameters about which very little is known such as frequency of injection and number of IDUs present at each sharing event.

Kretzschmar & Wiessing, (1998) describe a stochastic simulation model that models the spread of HIV in social networks of IDUs. The model distinguishes between stable ‘buddy’ relationships in which injecting equipment is shared on a regular basis and incidental risk contacts with strangers. The authors consider the effect of a reduction in sharing frequency or the effect of administering an Acquired Immune Deficiency Syndrome (AIDS) test to infected individuals on the incidence and prevalence of HIV over time the results from which are discussed below.

Peterson *et al.*, (1990) use a stochastic micropopulation model implementing Monte Carlo techniques that describes a community of IDUs to demonstrate the effects of social networks on HIV transmission and the importance of prevalence levels in assessing the effectiveness of interventions in the IDU population. This complex model consists of three interacting models, a model of HIV disease progression within an infected individual, a model describing the heterogeneity of injecting drug use within the IDU community, and a model of the social networks describing the pattern of equipment sharing by IDUs. However a problem with this approach is the amount of data required to parameterise a complex model such as this, indeed authors themselves consider a 'generic' IDU population in which typical parameter values that are reported across the literature from many studies are applied rather than values estimated from one specific IDU population.

A landmark paper by Kaplan, (1989) referred to from here on as 'Needles that kill' was one of the first papers to model the transmission of HIV via shared drug injecting equipment. This model describes the interaction between infected needles and infected IDUs. The author initially describes a homogenous model of an IDU population of constant size in which IDUs visit shooting galleries. The model considers how the probability of exposure to HIV and the prevalence of intravenously transmitted HIV within the IDU population may vary over time. The author then takes this model forward and introduces heterogeneity in the form of varying the rate that IDUs visit shooting galleries across the IDU population. The model is extended to incorporate the cleansing or bleaching of injecting equipment showing the impact that this may have on HIV prevalence. The authors also propose a method of reformulating the model to account for the inactivation of HIV infectiousness on infected needles over time. An application of the 'Needles that kill' model was demonstrated by Kaplan & O'Keefe, (1993) to evaluate the impact of the New Haven needle exchange on the HIV infection rate. A syringe tracking and testing system that provided data for the 'Needles that kill' model was developed. Applying this data the model estimated that the needle exchange reduced the HIV infection rates among IDUs using the exchange by 33%. This result provides strong

evidence of the validity of a needle exchange as an intervention measure to target the IDU population and reduce the transmission of BBVs.

In many cases the modelling in this field has concentrated on the examination of the important parameters that make the greatest contribution towards the transmission of BBVs. This is often done out of necessity as the data describing a specific IDU population required to parameterise a model is often difficult to obtain. In the case of BBVs and the IDU population, one of the modelling objectives is always to help understand the basic dynamical epidemiological processes underlying the spread of BBVs amongst sharing IDUs (Greenhalgh & Hay, 1997). Using a simple model Mather & Crofts, (1999) show that the rate that HCV spreads through a population of IDUs is extremely sensitive to the interaction rate between IDUs and to the probability of infection through a single contact with an infective. Kretzschmar & Wiessing, (1998) show the importance of IDUs sharing injecting equipment with strangers on the prevalence of HIV while Atkinson, (1996) shows the importance of clean needles and frequency of injecting in the prevention of the transmission of HIV. These models are often used to inform as to the parameters that have the largest impact on BBV transmission (Mather & Crofts, 1999; Kretzschmar & Wiessing, 1998; Atkinson, 1996; Peterson *et al.*, 1990).

There are some questions that often cannot be answered through the collection of data alone and in these circumstances modelling can play a useful role. For example Kaplan & Heimer, (1992) used the model described in 'Needles that Kill' in conjunction with data collected from the New Haven, Connecticut legal needle exchange programme to calculate the probability of HIV infection per injection with a contaminated syringe, estimating this to be approximately 0.067. Whereas Kretzschmar & Wiessing, (1998) were able to show through modelling that in populations where IDUs are part of a relatively stable social network, sustain steady partnerships and friendships, and confine their sharing of equipment to those persons they know well, HIV is given less of an opportunity to reach higher levels of prevalence. Modelling studies are a useful way of estimating the past and future trends of disease prevalence and incidence. An example of this can be seen with

Murray *et al.*, (2003) who describes the past and future trends of the incidence and prevalence of HCV and HIV within the IDU population of Australia.

A major problem with modelling the IDU population is that the data required to capture the true characteristics of the whole population is often difficult to obtain (Blower & Medley, 1992). The issues of data must be considered during model design, an overcomplicated model that considers too many subpopulations will result in a model that is impossible to parameterise. While models that consider the flows between subgroups of IDUs depending on their level of risk behaviour (Esposito & Rossi, 2004; Peterson *et al.*, 1990) and their contact with services (Esposito & Rossi, 2004) may seem attractive, to actually parameterise models such as this is often impossible. To avoid problems such as these, a generic IDU population describing a 'typical' IDU population can be used with which to parameterise the model (Kretzschmar & Wiessing, 1998; Atkinson, 1996), leaving the possibility of modelling a true population aside until accurate data become available. Other typical solutions to the problem of hard to obtain data include assuming that IDU population is of constant size over time (Kretzschmar & Wiessing, 1998; Iannelli *et al.*, 1992) or else assuming the IDU population is at steady state (Yakowitz, 1994).

To remove some of the problems associated with data collection, it is possible to consider the IDU population as being homogenous meaning there is no core-group of high risk individuals. This has the advantage in that fewer data are required to parameterise the model, and results can be obtained more quickly from a relatively simple model. This is best emphasized by the model described by Murray *et al.*, (2003), here the authors use a simple homogeneous model to make estimations in the trend of the HIV and HCV prevalence and incidence in the IDU population in Australia and their variation over time. While Kaplan & O'Keefe, (1993) use a homogeneous model to show the possible effects that a needle exchange has on the incidence of HIV. Kretzschmar & Wiessing, (1998) describe a homogeneous population regarding risk behaviour i.e. all individuals have the same propensity to borrow and share needles. The authors argue for this approach by pointing out that for any heterogeneity implemented into the model mixing rates between the different

subgroups must be defined and no information that could inform this was available to the authors in the population under consideration.

The introduction of heterogeneity into a model enables a system to be more realistically modelled and allows for the effects of potential targeted intervention measures to be more closely examined. The most common way to introduce heterogeneity into transmission models is to consider the variation in the rates that persons make contacts where the contact can lead to the potential transmission of infection (Anderson & May, 1991). In this case the contact would involve the risky behaviour associated with the sharing of needles and injecting paraphernalia. This might take the form of considering whether an IDU shares at a high or low rate (Arca *et al.*, 1992; Atkinson, 1996), whether an IDU shares with 'buddies' or strangers (Blower *et al.*, 1991), whether an IDU uses shooting galleries or not (Peterson *et al.*, 1990), or whether syringes are shared among partners or not (Allard, 1990). Heterogeneous mixing by gender has also been considered (Vickerman & Watts, 2002; Arca *et al.*, 1992; Blower *et al.*, 1991), and this is particularly useful when considering the additional effect of heterosexual transmission between the IDU and non-IDU populations. Mather & Crofts, (1999) describe heterogeneity in the IDU population by describing each sub-group in terms of its initial HCV prevalence and probability of infection through sharing needles. However the authors' approach is particularly unconvincing as they assume that there is no interaction between the different sub-groups of the population. Greenhalgh & Lewis, (2002) and Lewis & Greenhalgh, (2001) approach heterogeneity by considering the variable infectivity of HIV depending upon the time since infection, in both cases the authors expand on 'Needles that Kill' and apply three-stage infectivity to both addicts and needles. To emphasise that over complicated models do not always have an advantage over simpler models, Iannelli *et al.*, (1997) compared models of both homogeneous and heterogeneous contact within an IDU population finding that the model fit to the data for both models was similar.

An individual based or micropopulation model is an alternative approach to the modelling of the IDU population (Mather & Crofts, 1999; Kretzschmar & Wiessing, 1998; Atkinson, 1996; Peterson *et al.*, 1990). Atkinson, (1996) describes an IDU



population of 100 users that interacts with a population of needles with each addict having a variable sharing and injecting rate. The model informs as to the percentage of addicts that may become infected from HIV over time depending on their injecting frequency and their efforts at cleaning needles. The author's results show the importance of cleaning needles on the transmission of HIV. Peterson *et al.*, (1990) uses a micropopulation model to describe HIV infection in an IDU population showing the importance of prevalence levels in assessing the effectiveness of interventions that target IDUs. As already discussed authors frequently use typical parameter values reported across the literature rather than values estimated from one specific population to describe a generic or general IDU population (Atkinson, 1996; Mather & Crofts, 1999), and this probably emphasizes most clearly the difficulties associated with a model of this type. To precisely parameterise an actual IDU population on an individual level, describing the characteristics of IDUs and their interaction with each other is obviously prohibitive and this is why authors will frequently describe a generic population in which parameter estimates reported across the literature are used to describe an IDU population rather than values estimated from one specific population.

#### 1.6.2 Modelling prison populations

In various applications previous studies have attempted to model the prison population. Two previous studies that consider prison populations from the US are cost effectiveness studies examining the cost-effectiveness of HBV vaccination of prison inmates and combined HAV and HBV versus HBV vaccination for US prison inmates (Pisu *et al.*, 2002; Jacobs *et al.*, 2004). Both of these models consider hypothetical cohorts of a fixed number of prisoners entering prison at age 25 years of age with the prison population being described in the context of imprisonment in a US setting. While this approach is useful for simplicity it prevents the option of considering age dependent health interventions. The authors acknowledge model limitations based on the data sources describing the prison costs, HBV incidences outside and inside prison, and the rates of release and recidivism. In both cases the

authors estimate that HBV vaccination and HAV/B versus HBV vaccination in prisons are generally cost-effective.

A third study considers a model describing the HIV transmission in New South Wales (NSW) prisons (Dolan *et al.*, 1998). This model takes the model proposed in 'Needles that Kill' (Kaplan, 1989) and modifies it to incorporate flows of inmates into and out of prison. This deterministic model describes the interactions between inmates that are IDUs and needles circulating within prison with the HIV prevalence being considered in both populations. The author's assume that the rate that infected IDU inmates leave prison is equal to the overall inmate removal rate in other words IDUs and non-IDUs have the same imprisonment characteristics. Which given the mounting evidence that suggests that IDUs and non-IDUs have different offending characteristics (section 1.4 and Chapter 3) this is certainly a potential shortcoming of this approach. Using this model the authors are able to see the impact of cleaning needles in prisons, the infectivity of needles, and the HIV prevalence of IDUs entering prison on the number of IDU inmates infected per year. Although once again as this model is not age structured this prevents the examination of the impact of age dependent intervention measures.

The Home Office which is a government department of England and Wales uses modelling techniques to estimate the size of the prison population into the future. This model uses as inputs views of future sentencing trends including changes in custody rates and average custodial sentence lengths, and the impact of government implemented legislation. Typically when reporting model results three alternative scenarios are investigated. These assume either that observed recent sentencing trends continue into the future or that there is an increase or decrease in custody rates and average custodial sentence lengths respectively (de Silva *et al.*, 2006). The validity of the Home Office model is often vindicated by the closeness of the predicted prison population size to its actual size through time.

Finally two complex theoretical studies propose alternative approaches to the modelling of prison populations (Yakowitz *et al.*, 1996; Yablon, 1991). Yakowitz *et al.*, (1996) describes a numerical technique for a compartmentalized Markov

population process while Yablon, (1991) describes various stochastic models to represent the input output dynamics of prison populations, although in both these cases results obtained from the models are not described.

### 1.6.3 Modelling HBV transmission

As the modelling of HBV transmission in the IDU population will be the subject of a later chapter (Chapter 6), a review of previous modelling studies that describe the transmission of HBV is considered here.

The transmission of HBV within countries of high HBV endemicity (where the HBV prevalence in the population is high) have been considered in many previous modelling studies (Edmunds *et al.*, 1996b; Edmunds *et al.*, 1996a; McLean & Blumberg, 1994; Edmunds *et al.*, 1996c; Medley *et al.*, 2001; Zhao *et al.*, 2000). Due to the increased likelihood of becoming an HBV carrier at lower ages of infection (Edmunds *et al.*, 1993) models that consider populations with high HBV endemicity typically incorporate the transmission of HBV from mother to baby (Edmunds *et al.*, 1996b; Edmunds *et al.*, 1996a; McLean & Blumberg, 1994; Zhao *et al.*, 2000; Anderson & May, 1991). Considering populations of high HBV endemicity Medley *et al.*, (2001) examines the impact of a feedback mechanism where a higher prevalence of carriers leads to a lower average age of infection and this in turn leads to a high prevalence of carriers and so on.

Many previous modelling studies that have considered the transmission of HBV have incorporated sexual transmission (Williams *et al.*, 1996; Kretzschmar *et al.*, 2002; Edmunds *et al.*, 1996b; Edmunds *et al.*, 1996a; McLean & Blumberg, 1994). A previous study by Kretzschmar *et al.*, (2002) considers sexual behaviour and the transmission of HBV in the Netherlands focusing in particular on the impact of the immigration of HBV carriers from countries with higher prevalence, while Williams *et al.*, (1996) considers the transmission dynamics of HBV in the UK. In both cases the Netherlands and the UK being countries of low HBV endemicity.

Many studies have focused on the impact of various vaccination strategies on the transmission of HBV within the population under consideration (Kretzschmar *et al.*, 2002; Edmunds *et al.*, 1996b; Edmunds *et al.*, 1996a; Zhao *et al.*, 2000; Williams *et al.*, 1996). Zhao *et al.*, (2000) found that the key to controlling and eliminating HBV transmission in China was to find ways to immunize all infants throughout the country, while Edmunds *et al.*, (1996a) found that HBV eradication in the Gambia could be achieved by immunizing less than 70 per cent of infants. However in countries of low HBV endemicity mass vaccination was found to be a less attractive option. Examination of mass infant vaccination in the UK gave a poor effectiveness ratio (carriers prevented per cumulative dose of vaccine delivered) (Williams *et al.*, 1996). While in the Netherlands taking into account the prevalence of HBV carriage among immigrants and an age-dependent probability of becoming a carrier after infection, it was estimated that only a fraction of between 5% and 10% of carrier states could be prevented by universal vaccination (Kretzschmar *et al.*, 2002).

In previous models the impact of waning vaccine immunity has been considered (Edmunds *et al.*, 1996b; McLean & Blumberg, 1994). Edmunds *et al.*, (1996b) found that in a developing world setting providing that protection lasts in excess of 5-10 years, waning immunity following vaccination is unlikely to alter substantially the outcome of a mass vaccination programme.

In all cases the solution to the modelling of HBV transmission has been to use a deterministic model (Anderson & May, 1991; Williams *et al.*, 1996; Kretzschmar *et al.*, 2002; Edmunds *et al.*, 1996b; Edmunds *et al.*, 1996a; Edmunds *et al.*, 1996c; Medley *et al.*, 2001; McLean & Blumberg, 1994; Zhao *et al.*, 2000). This can be justified as the populations under consideration are usually large and do not have small numbers of susceptibles or infectives in which individual random events may affect the outcome.

IDUs are at high risk from HBV infection although to the author's knowledge no previous modelling studies have modelled the transmission of HBV within the IDU population. However the previous examination of alternative approaches to the

modelling of sharing and transmission of other BBVs suggest many approaches that could easily be applied to HBV transmission in the IDU population.

## **1.7 Objectives**

The objective of this thesis is to gain a greater understanding of the characteristics of the IDU population and its risk of BBV infection. Beginning with the parameterisation of a model describing the flow of IDUs through prisons in England and Wales a number of modelling approaches will be applied to investigate the effectiveness of a range of intervention measures that target IDUs in a prison setting. As part of the parameterisation of a model of the flow of IDUs through prisons, the age-specific rates at which IDUs start and stop using drugs must be estimated. This is the subject of Chapter 2.

## **CHAPTER 2 - MODELLING THE CHARACTERISTICS OF THE MALE INJECTING DRUG USER POPULATION IN ENGLAND AND WALES**

### **2.1 Aims and introduction**

- To estimate the age specific rate that IDUs leave the IDU population and how these may have evolved over time.
- To determine a distribution that describes the age that IDUs start injecting and investigate how this may have evolved over time.
- To investigate the incidence of injecting drug use and how this may have evolved over time

Understanding the characteristics of the IDU population is of major public health importance (Hutchinson *et al.*, 2006). Information on, for instance, the age-specific rates at which individuals start and stop injecting drugs can inform policy-making, particularly strategies aimed at the prevention of drug misuse (Home Office, 2002b).

The aim of this chapter is to propose a method in which key parameters that contribute towards the characteristics of the IDU population can be estimated from a data set such as the UAPMP surveys described in section 1.2. These key parameters can then be taken forward and applied in both modelling applications and to inform policy-making, as will be seen here where these results will be used during the parameterisation of a model describing the flow of IDUs through prisons (Chapter 3). Of particular interest are the age specific rates at which IDUs start and stop injecting drugs and how the incidence of injecting may have evolved over time. As the majority of IDUs are male (Hunter *et al.*, 2000) and the characteristics of male and female IDUs may differ considerably, only the male IDU population will be analysed, however the techniques described here can also be applied to the female IDU population.

## 2.2 Methods

### 2.2.1 Data

Using data from the UAPMP surveys undertaken in England and Wales as described in section 1.2. A current IDU is defined as a person that injected non-prescribed drugs in the previous four weeks (Section 1.1), all participating persons that had not injected within four weeks of the survey were excluded from the present analysis. Surveys from 1990 and 1991 were considered to be too small and so were discarded leaving ten complete consecutive surveys 1992-2001 which were available at the time of the analysis. In each survey male current IDUs with data on their current age (at time of the survey) and the age of their first injection were considered. The data were further constrained by limiting the current age range to be from 16-49, and the age of first injection to be from 13-45. Data outside these ranges were sparse and deemed too unreliable to be used.

### 2.2.2 Model

$C_{ijk}$  is the number of current IDUs in year  $k$ , aged  $i$  who started injecting at age  $j$ . (E.g.  $C_{30,20,1992}$  would be the number of 30 year old current IDUs in 1992, who started injecting when they were 20 years old.) Where:

$$C_{ijk} = f_{jy}g_yS_{ijk} \quad 2.1$$

where: -

$f_{jy}$  is the proportion of those persons who started injecting in year  $y$  that were aged  $j$

$g_y$  is the number of persons that started injecting in year  $y$

$S_{ijk}$  is the proportion of those persons that started injecting at age  $j$ , who are still injecting at age  $i$  in year  $k$ .

Those persons ( $S_{ijk}$ ) continuing to inject one year later

$$S_{i+1,j,k+1} = S_{ijk}(1 - \lambda_{ijk}) \quad 2.2$$

where  $\lambda_{ijk}$  the removal probability, is the proportion of IDUs with current age  $i$  and start age  $j$  being permanently removed from the surveyed injecting population in year  $k$ . This may be due to them stopping injecting for longer than 4 weeks, no longer reporting to services or because of deaths.

To make the results here applicable to the later chapters in this thesis (Chapter 3) the removal probability  $\lambda_{ijk}$  is converted into a removal rate  $\gamma_{ijk}$

$$\gamma_{ijk} = -\ln(1 - \lambda_{ijk}) \quad 2.3$$

The proportion of IDUs in contact with services may vary with injecting career length, for example it is known that IDUs with shorter injecting careers are likely to be underrepresented compared to more experienced users (Godfrey *et al.*, 2002). A measure of this under representation across all career lengths is incorporated in the model:

$p_{i-j}$  is the proportion of persons with career length  $(i-j)$  captured by a survey relative to a baseline career length.

The expected number of IDUs in survey year  $k$  of age  $i$  and start age  $j$  is

$$M_{ijk} = p_{i-j} C_{ijk} \quad 2.4$$

$Z_{ijk}$  is the probability than an IDU surveyed in year  $k$ , is of age  $i$  and start age  $j$

$$Z_{ijk} = \frac{M_{ijk}}{\sum_j \sum_i M_{ijk}} \quad 2.5$$



### 2.2.3 Parameterisation

It is assumed that both the proportion of persons starting injecting by age ( $f_{jy}$ ), the removal probability ( $\lambda_{ijk}$ ) and therefore the removal rate ( $\gamma_{ijk}$ ) do not vary with time ( $f_{jy}=f_j$ ,  $\lambda_{ijk}=\lambda_{ij}$ , and  $\gamma_{ijk}=\gamma_{ij}$ ). Both these assumptions will be examined during tests of sensitivity. It is also assumed that the removal probability ( $\lambda_{ijk}$ ) and therefore the removal rate ( $\gamma_{ijk}$ ) do not vary with the age that IDUs start injecting drugs ( $\lambda_{ij}=\lambda_i$ , and  $\gamma_{ijk}=\gamma_i$ ).

The absolute size of the male IDU population is not known and so it is not possible to calculate the number of males starting injecting each year. Therefore  $g_y$  is relative to some arbitrary fixed reference year detailed below.

As a starting point for analysis, an initial model was proposed with which to fit the data and this is defined as:

$f_j$  is described by a gamma distribution at age  $a$  with an offset  $\omega$ ,  $f(a-\omega) = \text{gamma}(\mu, \sigma)$

$p_{i-j}$  is grouped into the following injecting career lengths; <1, 1-2, 3-4, 5-9 yrs, and calculated relative to a fixed injecting career length of 10+ years = 1.

$g_y$  is grouped into eleven 2 year groups (1980-81, 1982-83 etc.) and is calculated relative to year group 1988-89 = 1000.

$\lambda_i$  is grouped into four age groups; 13-19 years, 20-24 yrs, 25-29 yrs, 30+ yrs

The initial model was fitted to the data as follows:

Within each survey year  $k$ , the data,  $D_{ij}$ , (count of the number of IDUs surveyed at age  $i$ , with starting age  $j$ ) are assumed to follow a multinomial distribution. The log likelihood of the model given the data within year  $k$  is:

$$\log lik_k = \sum_{ij} D_{ijk} \log Z_{ijk} \quad 2.6$$

each survey is independent, therefore

$$\log lik = \sum_k \log lik_k$$

2.7

Then, maintaining the gamma distribution describing  $f_j$ , backwards step-wise elimination was used to reduce the number of strata describing  $g_y$ ,  $p_{i-j}$ , and  $\lambda_i$ . Nested models were compared by the difference in deviance and the degrees of freedom, which can be tested using a chi-squared test with degrees of freedom equal to the difference in degrees of freedom between models. For comparisons between non-nested models, i.e. such as in a case where a function is changed from piece-wise constant to linear, a comparison between the resultant deviances was made. This process lead to a final parsimonious model containing less parameters than the initial model. 95% confidence intervals (CI) were calculated using the profile likelihood method (Armitage & Colton, 1998).

A selection of the reduced models used during the step-wise elimination process is described below (only changes from the initial model are noted):

1. The initial model
- 2  $\lambda$  is described by a linear function with age.  $\lambda(a) = \max(\pi a + k, 0)$ .
- 3  $\lambda$  is described by a linear function with age up to a maximum and then constant thereafter.  $\lambda(a) = \min((\max(\pi a + k, 0), \nu))$ .
- 4 As model 3 above, except  $g_y$  is grouped into five 4 year groups (1980-83, 1984-1987, 1990-1993 etc.) and is calculated relative to the fixed year group 1988-1989 = 1000.
- 5 As model 3 above, except  $p_{i-j}$  is grouped into the following injecting career lengths; <1, 1-2, 3-9, and is calculated relative to a fixed injecting career length of 10+ years.
- 6 As model 3 above, except  $p_{i-j}$  is grouped into the following injecting career lengths; <1, 1-9, and is calculated relative to a fixed injecting career length of 10+ years.

## 2.2.4 Sensitivity Analysis

Sensitivity analysis involves systematically examining the influence of uncertainties in the variables and assumptions employed in an evaluation on the estimated results. It encompasses at least three alternative approaches (Briggs & Gray, 1999):

- *One way sensitivity analysis* systematically examines the impact of each variable in the study by varying it across a plausible range of values while holding all other variables in the analysis constant at their “best estimate” or baseline value.
- *Extreme scenario analysis* involves setting each variable to simultaneously take the most optimistic (pessimistic) value from the point of view of the intervention under evaluation in order to generate a best (worst) case scenario.

Frequently the components of an evaluation do not vary in isolation nor are they perfectly correlated, hence it is likely that one way sensitivity analysis will underestimate, and extreme scenario analysis will overestimate, the uncertainty associated with the results of an evaluation.

- *Probabilistic sensitivity analysis*, which is based on a large number of Monte Carlo simulations, examines the effect on the results of an evaluation when the underlying variables are allowed to vary simultaneously across a plausible range according to predefined distributions. These probabilistic analyses are likely to produce results that lie between the ranges implied by one way sensitivity analysis and extreme scenario analysis and therefore may produce a more realistic estimate of uncertainty.

The sensitivity analysis of the final model proposed here took three approaches.

1. To test the assumption that the removal probability ( $\lambda_r$ ) is constant over time. The data from surveys 1992-1996 and 1997-2001 were each modelled separately with the results compared to each other and that obtained from all surveys 1992-2001.

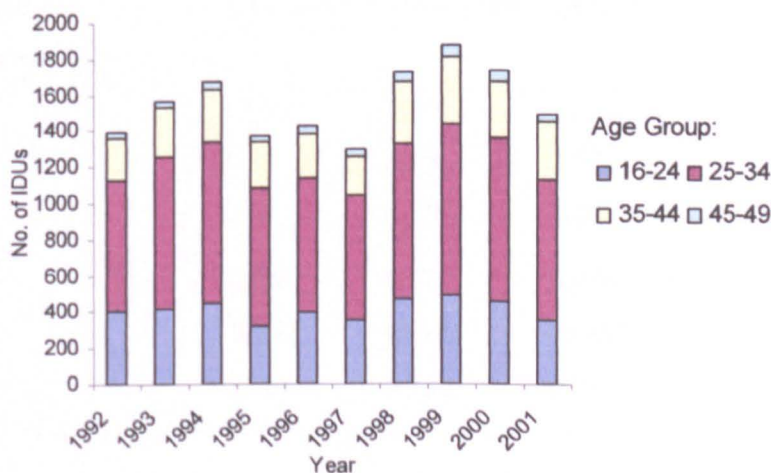
2. To test the assumption that the function describing the proportion of persons starting injecting by age ( $f_j$ ) is constant over time. Again the data from surveys 1992-1996 and 1997-2001 were each modelled separately with the results compared to each other and that obtained from all surveys 1992-2001.
3. To test the sensitivity of  $p_{i-j}$  and  $g_y$ , 95% CIs were calculated for each of the parameters describing these functions.

## 2.3 Results

### 2.3.1 Data

Considering IDUs that started injecting from 1980 onwards, there were approximately 1,500 male current IDUs in each annual survey with an overall total of 13,536 records analysed (Figure 2.1). The mean age of an IDU surveyed across all years was 27.9 years old, the mean age of first injection was 21.2 years, with a mode of 18 years of age. Across surveys 1992-2001 the average injecting career of an IDU calculated using the total injecting years and the total number of records was found to be 5.82 years. Including the injectors that started prior to 1980, for surveys 1992-2001, the mean age of an IDU surveyed across all years was 29.3 years, the mean age of first injection was 20.8 years, and the average injecting career was 8.56 years.

Figure 2.1 - Age breakdown of the current IDUs starting injecting from 1980 onwards



### 2.3.2 Model Fit

The calculated model parameters for the parsimonious model are shown in Table 2.1 and Table 2.2 with CIs where appropriate. Table 2.3 shows the results of the fitting procedure. The deviance of the  $n$ th reduced model as described in the Parameterisation section is denoted  $D_n$ . Models 1, 2, and 3 examined the removal probability with model 3 using a linear removal probability up to a maximum being selected. As none of these models were nested, only a direct comparison between each deviance could be made. Model 4 considers a reduction in the number of parameters describing the function  $g_y$  however this was found to give a significantly less good fit than model 3 ( $D_4 - D_3 = 112.9$ , 5 d.f.,  $p < 0.001$ ). Model 5 considers a reduction in the number parameters describing  $p_{i,j}$ , this was found to give a significantly better fit than model 3 ( $D_5 - D_3 = 1.9$ , 1 d.f.,  $p = 0.165$ ). A further reduction in the number of parameters describing  $p_{i,j}$  was also investigated (Model 6), however this was found to give a significantly less good fit than model 5 ( $D_6 - D_5 = 19.0$ , 1 d.f.,  $p < 0.001$ ). Model 5 was therefore taken to be the parsimonious model. Figure 2.2 shows for each survey the complete data set (bars) and the model fit (lines) for the parsimonious model, showing that the parsimonious model provides a good fit to the data.

Table 2.1 - Parsimonious Model Parameters describing functions  $f(a-\omega)$  and  $\lambda(a)$ .

Model	1992-2001	1992-1996	1997-2001
Parameters			
$\omega$	12.58	12.92	12.32
$\mu$	3.61	3.58	3.57
$\sigma$	3.32	3.19	3.53
$\pi$	0.020	0.027	0.016
$\kappa$	-0.353	-0.504	-0.287
$\nu$	0.310	0.332	0.319

*When considering data from 1992-2001, 1992-1996, and 1997-2001*

Table 2.2 - Model parameters describing the parsimonious model for functions g and  $P_{i-j}$ .

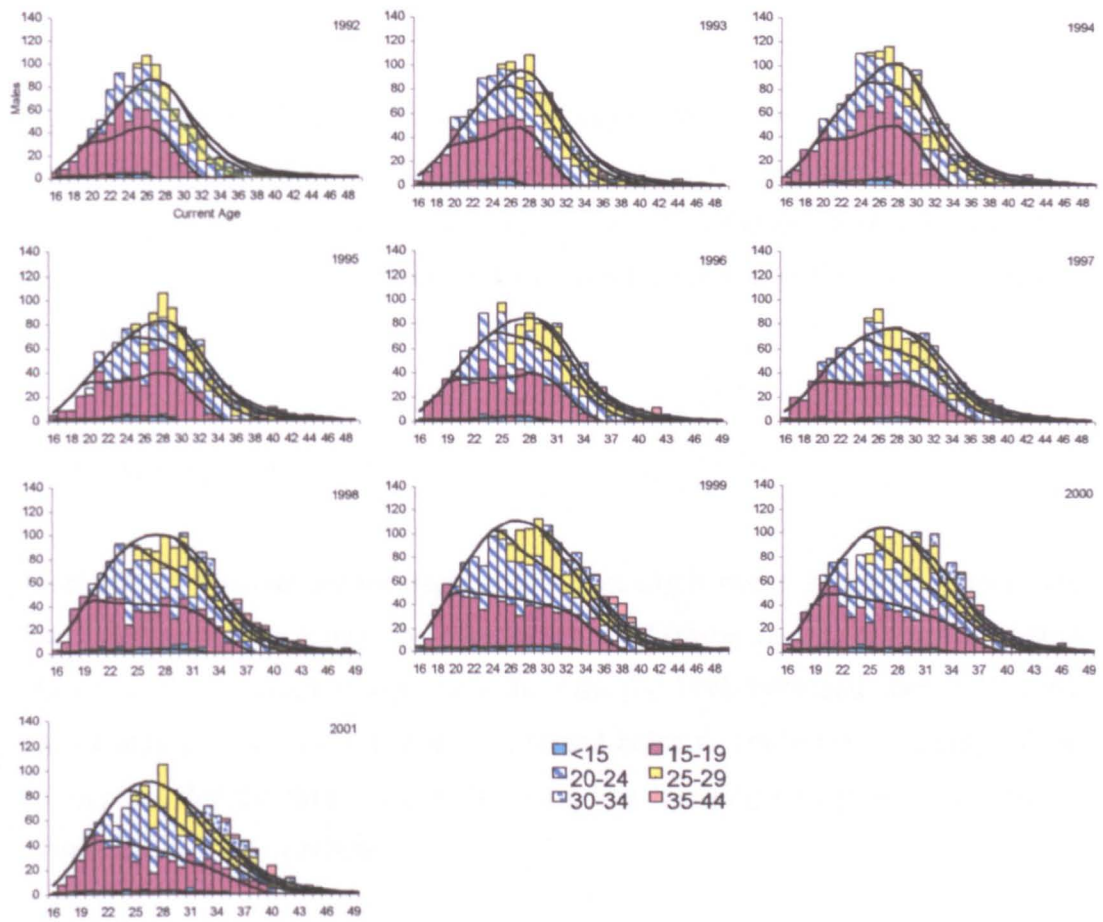
	Best Fit	95% Confidence Interval
$g_y$		
1980-1981	3479	3008-3734
1982-1983	2907	2696-3251
1984-1985	2069	1882-2139
1986-1987	1438	1326-1558
1988-1989	1000	Fixed
1990-1991	927	860-999
1992-1993	743	683-812
1994-1995	670	596-735
1996-1997	622	551-709
1998-1999	485	418-589
2000-2001	334	272-413
$P_0$	0.733	0.660-0.794
$P_{1-2}$	1.000	0.924-1.000
$P_{3-9}$	0.881	0.832-0.918
$P_{10+}$	1.00	Fixed

*For all data 1992-2001*

**Table 2.3 - Goodness of fit of initial and reduced models**

<b>Model</b>	<b>d.f.(n=3,051)</b>	<b>Deviance (D<sub>n</sub>)</b>
<b>1 (initial model)</b>	<b>3,032</b>	<b>5,553.2</b>
<b>2</b>	<b>3,034</b>	<b>5,586.4</b>
<b>3</b>	<b>3,033</b>	<b>5,514.9</b>
<b>4</b>	<b>3,038</b>	<b>5,627.8</b>
<b>5</b>	<b>3,034</b>	<b>5,516.8</b>
<b>6</b>	<b>3,035</b>	<b>5,535.8</b>

Figure 2.2 – Age specific data for each survey year 1992-2001 broken down by the age of first injection with model fit.





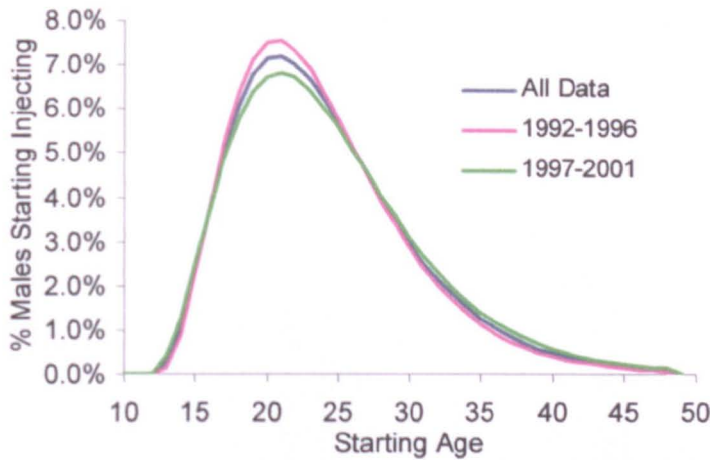
### 2.3.3 Under ascertainment ( $p_{i-j}$ )

The values obtained for  $p_{i-j}$  (Table 2.2) suggest that there is evidence of under ascertainment particularly in the new initiates, i.e. those injectors whose injecting starting age ( $j$ ) is the same as their current age ( $i$ ). Although there was also some evidence of under ascertainment for those injectors with injecting career lengths of up to 9 years.

### 2.3.4 Starting with age ( $f_j$ )

Over 50% of injectors are estimated to start injecting between 18 and 25 years of age and less than 15% start injecting over 30 years old (mean age of starting = 21 years) (Figure 2.3). Considering separately the data for 1992-1996 and then 1997-2001 shows only a small difference in results and helps to confirm the validity of the assumption that the proportion of IDUs starting injecting by age does not change within this data set over time.

Figure 2.3 - Function  $f_j$ : The proportion of IDUs starting injecting by age.

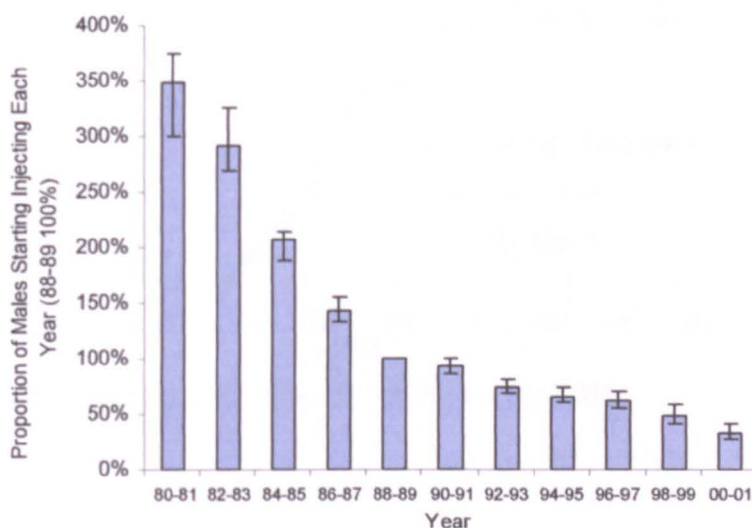


*Using data from 1992-2001, 1992-1996, and 1997-2001.*

### 2.3.5 The relative number of males starting injecting over time ( $g_y$ )

The relative number of males starting injecting each year, function  $g_y$ , is shown in Figure 2.4. The graph compares the number of males starting injecting between each year assuming that 1,000 injectors started in 1990. If for example in a given year the number of males starting injecting was 2000, this would mean that the model estimates that twice the number of males started injecting in that year compared to 1990. The result presented here shows a peak of persons starting injecting in the early 1980s. From then there was a drop in the number of males starting injecting until 1990 after which there has been a broad stabilization (or perhaps a small drop).

Figure 2.4 - Function  $g_y$ . The relative proportion of males starting injecting each year.

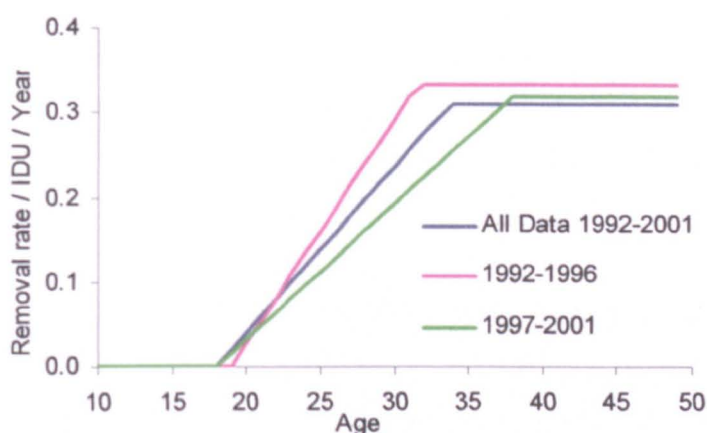


*Assuming 100% in 1988-89 with 95% CIs*

### 2.3.6 Removal Rate

The removal rate for the parsimonious model were found to be linear with age up to a maximum and then constant thereafter. The initial piece-wise constant distribution described by the initial model was found to give a much inferior fit to the data. The results suggest that the older an IDU is, the more likely it is he will be removed from the IDU population up to around 30-35 years of age, thereafter the removal rates appear to remain constant (Figure 2.5). Although the removal rates for male injectors under 19 years of age are estimated to be zero, it is acknowledged that there is a chance that a younger IDU may leave the IDU population. For older data (1992-1996) the removal rate was found to be higher across all age groups aged 19 and above, this suggests a potential change in injecting behaviour through the 1990s. If it is assumed that the removal rates accurately reflect the rate that IDUs either stop injecting or die, the results obtained from the removal probabilities ( $\lambda_i$ ) and the function describing the age of starting ( $f_j$ ) can be used to calculate the average injecting career of an IDU. From the parsimonious model the average injecting career was found to be 5.97 years (5.56 – 6.60 yrs; 95% CI).

Figure 2.5 - The age-specific rate that IDUs leave the IDU population per year ( $\gamma_i$ ).



Using data from 1992-2001, 1992-1996, and 1997-2001.

## 2.4 Discussion

The work proposes a method in which key parameters that contribute towards an increased understanding of the characteristics of the IDU population can be estimated from a data set consisting of a sequence of IDU surveys. In this case the data set was ten consecutive UAPMP surveys (1992-2001) of current IDUs with information on their current age, age at the time of the survey, and their age at first injection (section 1.2).

Many epidemiological surveys have sought to gain an insight into the characteristics of the IDU population, and some estimates of the rates that IDUs start and stop using drugs have been made elsewhere (Murray *et al.*, 2003; Pollack, 2001; Law *et al.*, 2001; Kaplan, 1989) (section 1.1.1) however this work is novel in that it provides a method by which an age specific removal rate, a distribution for the age specific starting age, and the trend in the injecting incidence of time can be estimated from data such as the UAPMP surveys of IDUs in England and Wales (Health Protection Agency *et al.*, 2005).

As a starting point for analysis an initial model was proposed consisting of a number of parameters describing each model function. It is normal for a full model to be used

at this stage and it is acknowledged that the initial model could have been described by many more parameters however this was not done for two reasons. The computing power required to manipulate a model such as this would have been prohibitive and there is a danger that a 'many parameter' model may lead to 'over fitting' of the data.

The model predicts the most likely starting age of a male IDU to be 21 years old (Figure 2.3) and this result compares well with the observed mean age of first injection of 21.2 years. It was also found that over 50% of injectors are estimated to start injecting between 18 and 25 years of age. It was assumed in the model structure that this function did not change over time. The similar results obtained when the model was fit to data from two separate time periods, i.e. 1992-1996 and 1997-2001 gives confidence to the validity of this assumption.

The removal rates obtained from the model (Figure 2.5) show that as an injector's age increases his chance of leaving the IDU population increases up to a plateau at around 30-35 years of age, after which the rate is constant. In the case of the data examined here, an IDU may leave the IDU population because he has died, stopped injecting, or stopped reporting to services. While it is impossible to know which, the results here do point to an increasing injecting cessation rate with age followed by constant cessation behaviour in older injectors.

It is acknowledged that the natural death rate increases with age and the constant removal rate in the older age groups do seem to contradict this. However the small increase in the death rate for ages 35-49 is insignificant compared to the high constant removal rate across the same age group.

Assuming the removal probability is a reasonable approximation of the probability that IDUs either stop injecting or die, the average expected injecting career length from the parsimonious model was found to be 5.97 years (5.56 - 6.60 yrs; 95% CI). This is similar to the average injecting career length obtained from the crude data of 5.82 years.

The number of males starting injecting each year shows a high incidence of injecting in the early 1980s followed by a sharp decline (Figure 2.4). This fits well with the effects of individual and social concern following the sudden emergence of AIDS and HIV infection in IDUs. Throughout the 1990s there appears to have been a fairly stable incidence of new male injectors. This is also in agreement with other studies. For instance, Hickman *et al.*, (2001) estimated the incidence of heroin use from 1991-1998, and found a stable incidence during this period. The slight reduction in the number of males starting injecting in 2000-2001 coupled with an increase in the average injecting career length of an IDU in more recent years (1997-2001 lower removal rate) may be indicative of a change in the nature of the IDU population with more 'problem' rather than casual users.

The methods described here provide a technique by which key parameters can be obtained that will contribute towards a greater understanding of the IDU population and its characteristics. As has been shown here, in each given moment the population of active IDUs is a mix of injectors who have been injecting for a different numbers of years and this range is very relevant in terms of the implementation of targeted prevention strategies.

This chapter concludes analysis that has considered the characteristics of the IDU population. Having obtained age-specific rates that IDUs start using drugs and leave the IDU population this work can be taken forward and contribute to the parameterisation of a model describing the IDU population and its flow through prisons. This will be the major focus of Chapter 3.

**The research in this chapter has been published in full in the following peer reviewed article:**

**Sutton, A. J., Gay, N. J., Edmunds, W. J., Andrews, N. J., Hope, V. D., & Gill, O. (2005). Modelling the Characteristics of the Male Injecting Drug User Population in England and Wales. *International Journal of Drug Policy* 16, 176-182**

## **CHAPTER 3 - MODELLING THE FLOW OF INJECTING DRUG USERS THROUGH PRISONS IN ENGLAND AND WALES**

### **3.1 Aims and Introduction**

- To parameterise a model describing the flow of IDUs and non-IDUs through prisons in England and Wales so that this can then be applied to investigate a variety of alternative intervention measures that target IDUs in a prison setting.
- To provide a greater understanding of the offending characteristics of the IDU population and how this compares to non-IDUs.

To estimate the impact of intervention measures that target the IDU population in a prison setting it is of importance to gain an understanding of the rate that IDUs flow through prisons. The number of IDUs that appear on reception into prison and their length of prison stay will have an impact on the success of any prison based intervention targeting the IDU population. To address questions such as this a model is required which describes the turnover of IDUs and non-IDUs through prison. This can inform as to the rates that IDUs and non-IDUs pass through prisons and provide a greater understanding of the offending characteristics of the IDU population. The chapter here describes the parameterisation of the model of the flow of IDUs through prisons in England and Wales.

The estimation of the model parameters is described here and these are used in conjunction with the rates that IDUs start injecting and leave the IDU population estimated in Chapter 2 to fully parameterise the model. Sensitivity analysis of key model parameters is undertaken in the context of the HBV prison vaccination programme in England and Wales. This is shown in Chapter 4.

## 3.2 Methods

### 3.2.1 Population

The purpose of this model is not to make detailed projections regarding the prison population over time and so we assume that both the male prison population and the total male population (females are not considered) of England and Wales are stable. Mortality is assumed to be zero until 74 years and infinite thereafter producing a fixed life expectancy of 75 years. The model considers only males aged 15–74 years, stratified into 60 age cohorts. Persons enter the model at the start of the year into the first age cohort (at 15 years of age). Thereafter individuals change age cohorts at the beginning of each year. It is assumed that the total number of persons in each age group is the same and is constant over time.

### 3.2.2 Model structure

The model describes the flow of IDUs and non-IDUs through prison. It is an age-structured deterministic model based on a set of ordinary differential equations illustrated in Figure 3.1 with parameter definitions described in Table 3.1. Each mutually exclusive compartment represents a different status of imprisonment and injecting, and the arrows represent the flow of individuals between them. A person can either have never been to prison, be currently in prison, or have been previously imprisoned, and, can never have injected drugs, be a current IDU, or have been an IDU in the past. Prisoners are considered to be IDUs if they were current IDUs (injected in the previous 4 weeks) on reception into prison.

The rates of starting ( $\beta$ ) or stopping ( $\gamma$ ) injecting (as calculated in Chapter 2 in conjunction with an assumed IDU population size in the case of the start rates ( $\beta$ )) are assumed to be independent of prison status (never, currently or previously imprisoned). The rates at which individuals go to prison for the first time ( $\mu$ ), are discharged from prison ( $\rho$ ), and return to prison ( $\theta$ ) are assumed to be the same for non-IDUs and past-IDUs but may be different for current IDUs.



### 3.2.3 Mathematical Structure

The differential equations for the deterministic model are as follows:

$$\frac{dX_i}{dt} = -(\mu_i + \beta_i)X_i \quad 3.1$$

$$\frac{dY_i}{dt} = X_i\mu_i + Z_i\theta_i - (\rho_i + \beta_i)Y_i \quad 3.2$$

$$\frac{dZ_i}{dt} = Y_i\rho_i - (\theta_i + \beta_i)Z_i \quad 3.3$$

$$\frac{dXI_i}{dt} = \beta_i(XP_i + X_i) - (\mu_i^* + \gamma_i)XI_i \quad 3.4$$

$$\frac{dYI_i}{dt} = (XI_{ij}\mu_i^* + ZI_{ij}\theta_i^*) - (\rho_i^* + \gamma_i)YI_i + \beta_i(Y_i + YP_i) \quad 3.5$$

$$\frac{dZI_i}{dt} = \beta_i(Z_i + ZP_i) + YI_i\rho_i^* - ZI_i(\theta_i^* + \gamma_i) \quad 3.6$$

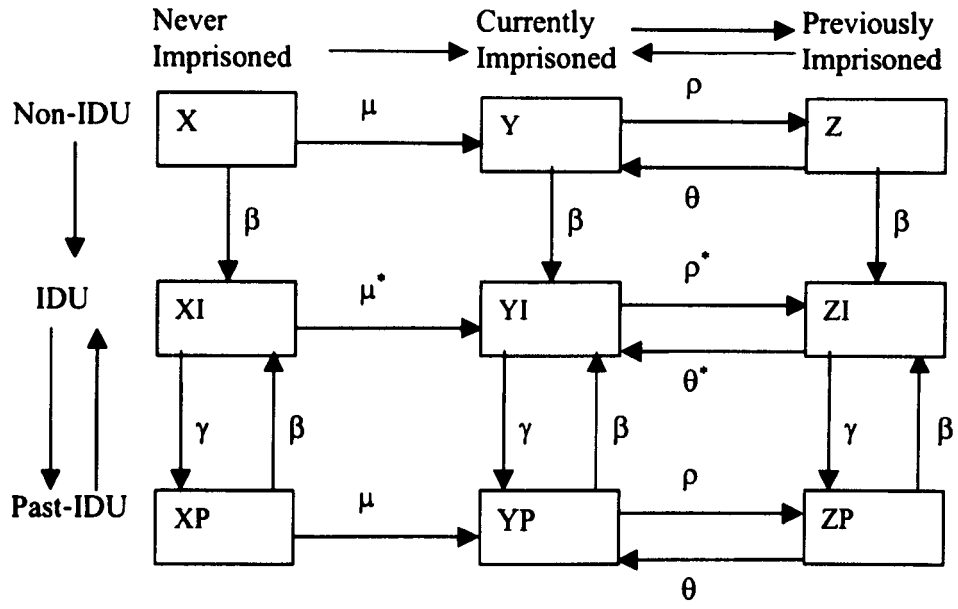
$$\frac{dXP_i}{dt} = XI_i\gamma_i - (\beta_i + \mu_i)XP_i \quad 3.7$$

$$\frac{dYP_i}{dt} = (XP_i\mu_i + ZP_i\theta_i) + YI_i\gamma_i - (\beta_i + \rho_i)YP_i \quad 3.8$$

$$\frac{dZP_i}{dt} = YP_i\rho_i + ZI_i\gamma_i - (\theta_i + \beta_i)ZP_i \quad 3.9$$

The number of individuals of age  $i$  who have never been imprisoned and are non-IDUs ( $X$ ), imprisoned non-IDUs ( $Y$ ), previously imprisoned non-IDUs ( $Z$ ), never been imprisoned IDUs ( $XI$ ), imprisoned IDUs ( $YI$ ), previously imprisoned IDUs ( $ZI$ ), never been imprisoned previous IDUs ( $XP$ ), imprisoned previous IDUs ( $YP$ ), previously imprisoned previous IDUs ( $ZP$ ). The different parameters determining the rates of flow between imprisonment states and IDU status are described in Table 3.1.

Figure 3.1 - Flow diagram of the age specific turnover of IDUs and non-IDUs in England and Wales repeated for each of the 60 age groups.



The mutually exclusive compartments represent the different imprisonment and IDU states. Arrows represent the flows between the states

Table 3.1 - Baseline parameter estimates and definitions.

<i>Symbol</i>	<i>Definition</i>	<i>Baseline Value (all rates: / person / year)</i>
$\gamma$	The rate that current IDUs stop injecting	Age specific
$\beta$	The rate that non-IDUs and past-IDUs start injecting	Age specific
$\mu$	The rate that non-IDUs and past-IDUs go to prison for the first time	Age specific
$\mu^*$	The rate that IDUs go to prison for the first time	Age specific
$\rho$	The rate that non-IDUs and past-IDUs are discharged from prison	Age specific
$\rho^*$	The rate that IDUs are discharged from prison	Age specific
$\theta$	The rate that non-IDUs and past-IDUs return to prison having been previously imprisoned	Age specific
$\theta^*$	The rate that IDUs return to prison having been previously imprisoned	Age specific
$\tau$	Average injecting career length dependent on injecting starting age (Chapter 2)	5.97 years
	Size of the male IDU population	120,000 (de Angelis <i>et al.</i> , 2004)
	Size of the male prison population	61,775
	Total male population	Variable with age, (Office of National Statistics, 2003)

### 3.3 Model parameterisation and key findings

Where possible parameters were directly calculated from specific data sources ( $\gamma, \beta, \rho$ ) or were indirectly estimated by maximum likelihood from data on IDUs and prisons ( $\theta, \mu$ ). Age specific rates at which IDUs start and stop using drugs ( $\beta(a)$  and  $\gamma(a)$  respectively) were taken from analysis of the UAPMP surveys of current IDUs described in Chapter 2.

#### 3.3.1 Prison discharge rates ( $\rho(a)$ and $\rho_I(a)$ )

Data were taken from a survey of prisoners in 1997/8 (Weild *et al.*, 2000) describing the sentence length, the age, and the IDU status of prisoners from a cross section of prisons in England and Wales (Table 3.2). There are two difficulties in calculating the average length of imprisonment per spell of imprisonment for IDUs and non-IDUs from these data. The actual time served for a sentence will be less than the sentence length imposed, and a cross-sectional survey of prisoners' current sentence lengths is not representative of all admissions because the prisoners serving longer sentences will be over-represented.

Prison statistics 2001 (Home Office, 2002a) provide data on the average time served by length of sentence, and so data were adjusted from length of sentence to average time served. To allow for the over-representation of longer sentences in the prison survey, the number of prisoners for each length of sentence was weighted by  $1/(\text{average time served})$ . The discharge rate for each age group was then calculated (Table 3.3).

Table 3.2 – Data (1997-1998) from a cross section of prisons in England and Wales.

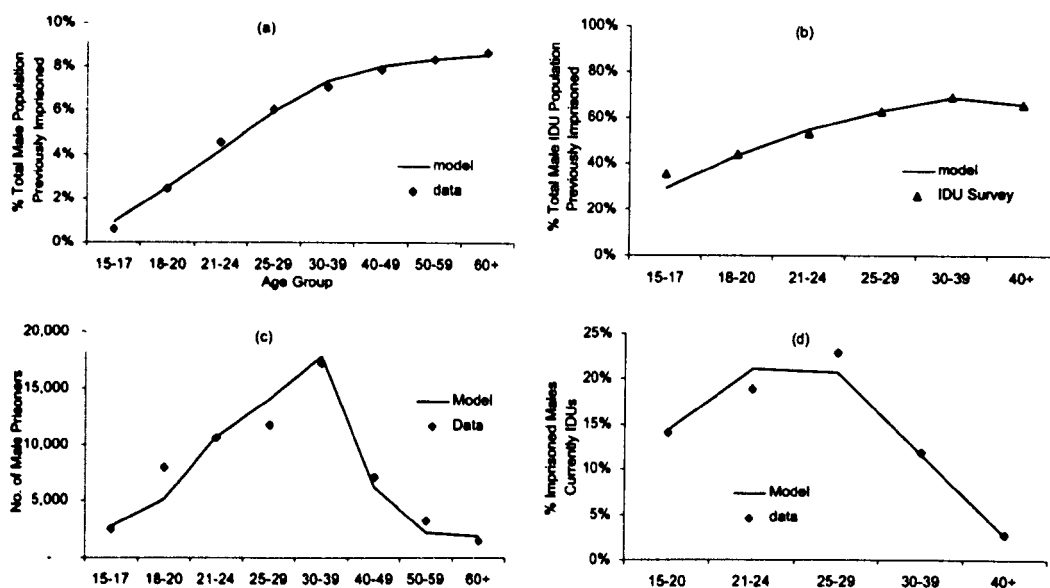
<i>Non-Injecting Drug Users</i>						
Young Offenders		Sentence				
Age	Remand	<3months	3-12months	1-3years	3+years	Total
<16	49	14	26	49	20	158
17	55	11	16	35	27	144
18-19	138	22	26	52	39	277
20-21	48	12	9	18	19	106
Total	290	59	77	154	105	685
Adult Prisoners						
Age	Remand	<3months	3-12months	1-3years	3+years	Total
<25	94	16	39	113	205	467
26-30	59	9	47	114	266	495
31-35	50	7	41	102	311	511
36-40	11	3	14	70	146	244
41+	25	11	38	100	458	632
Total	239	46	179	499	1386	2349
<i>Injecting Drug Users</i>						
Young Offenders		Sentence				
Age	Remand	<3months	3-12months	1-3years	3+years	Total
<16	1	1	0	0	0	2
17	0	0	1	2	0	3
18-19	3	0	0	0	1	4
20-21	1	0	0	1	0	2
Total	5	1	1	3	1	11
Adult Prisoners						
Age	Remand	<3months	3-12months	1-3years	3+years	Total
<25	40	3	5	26	36	110
26-30	39	3	15	29	63	149
31-35	24	0	6	10	40	80
36-40	4	0	1	6	12	23
41+	3	0	3	0	12	18
Total	110	6	30	71	163	380

(Weild et al., 2000)

### 3.3.2 Imprisonment Rates ( $\mu(a)$ , $\mu_I(a)$ , $\theta(a)$ , and $\theta_I(a)$ ).

The rate of first time imprisonment for IDUs and non-IDUs, and the rate of repeat imprisonment for IDUs and non-IDUs were estimated concurrently by fitting the model to data described in Figure 3.2 by maximum likelihood (section 3.3.3) keeping previously estimated parameters (discharge rates, IDU start and stop rates) at their base-case level.

Figure 3.2 - Model fit to age specific data.



(a) The percentage of the male population that has ever been imprisoned (Prime *et al.*, 2001), (b) The percentage of the male IDU population that has ever been imprisoned (2001,  $n=3,904$  (Unlinked Anonymous Surveys Steering Group, 2002)). (c) The male prison population (Home Office, 2002a), (2001,  $n=61,775$ ). (d) The % of prisoners that are current IDUs (Weild *et al.*, 2000) ( $n=3,425$ ).

Figure 3.2 (d) shows the proportion of the male prison population that are current IDUs (Weild *et al.*, 2000). The original data for age group 15-20 years was 1.6% (11/708). From the UAPMP Survey 2001, 35% of 15-17 year old IDUs had been to prison and for the 18-20 year group the figure was even higher at 44%. Coupled with the fact that the young offender data were only obtained from one institution, it may be that this figure is not a true reflection of the proportion of imprisoned young offenders that are IDUs. Additional data of arrestees aged between 17 and 24 that were interviewed and urine tested for drugs whilst on arrest in police custody suites showed that rates of last-year use of heroin, crack and cocaine all stood at around 20% (Bennett, 2000). On the basis of these concerns an alternative arbitrary value of 14.1% was selected (100/708) as the base case however the effects of this selection are examined in the sensitivity analysis.

The full model was fitted using maximum likelihood applied to binomial data. The functions describing the first time and repeat reception rates were each examined separately to find an appropriate functional form. An iterative process in which various functional forms were applied and tested was used. Resultant deviances for each test were compared, with the functional form exhibiting the lowest deviance being selected.

### 3.3.3 Maximum likelihood fitting to binomial data

The model was fitted to the binomial data using maximum likelihood. The saturated likelihood ( $L^*$ ) and the model likelihood ( $L$ ) are defined as:

$$L^* = \sum_i (a_i \ln(P_i) + b_i \ln(1 - P_i)) \quad 3.10$$

$$L = \sum_i (a_i \ln(M_i) + b_i \ln(1 - M_i)) \quad 3.11$$

Where

$a_i$  is the observed number of positives (data) in age group  $i$

$b_i$  is the observed number of negative (data) in age group  $i$

$$P_i = \frac{a_i}{a_i + b_i} \quad 3.12$$

$M_i$  is the modelled proportion positive in age group  $i$

Deviance for each data set (as shown in Figure 3.2) is:

$$D = 2(L^* - L) \quad 3.13$$

The above is repeated for each independent data set, with the deviance for each data set being summed to provide an overall deviance

### 3.3.3.1 Over-dispersion

Due to the size of the numerator in the prison population size, this dominates the binomial likelihood. The practical effect is that the model fit is also dominated by this part of the data. Despite this, no model gave a good fit to these data when using the binomial distribution. Therefore we introduced an over-dispersion parameter to this part of the data using the negative binomial distribution (McCullagh & Nelder, 1989). The over-dispersion parameter  $\phi$  was chosen to fix the deviance of that part of the data equal to its degrees of freedom.

#### Negative Binomial Maximum Likelihood

$Y_i$  = observed number of positives (data) for age group  $i$

$\mu_i$  = expected number of positives (model) for age group  $i$

$$L = \sum_i \left[ \log(\Gamma(y_i + \phi\mu_i)) - \log(\Gamma(\phi\mu_i)) + \phi\mu_i \log\left(\frac{\phi}{1 + \phi}\right) \right] \quad 3.14$$

Saturated likelihood  $\mu_i = y_i$

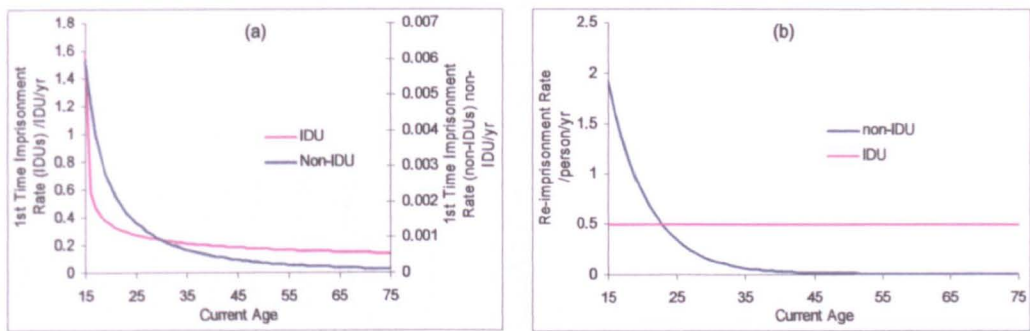
$$L^* = \sum_i \left[ \log(\Gamma(y_i + \phi\mu_i)) - \log(\Gamma(\phi\mu_i)) + \phi y_i \log\left(\frac{\phi}{1 + \phi}\right) \right] \quad 3.15$$

It was found as a consequence of applying the fitted model that the calculated values for the discharge rates for the IDU population resulted in lower repeat reception rates for IDUs compared to non-IDUs across all ages. IDUs are generally more likely to re-offend than non-IDUs (Seaman *et al.*, 2000), and it was found by assuming that the discharge rate for IDUs was the same for all age groups (at the 15-19 age group rate) that a higher re-imprisonment rate for IDUs could be achieved. An argument for this can be made when considering data from different types of prison from the prison survey. Considering data from only local prisons the average time spent in prison for an IDU across all age groups is 3.8 months, this was comparable to the 2.64 months for the 15-19 age group IDUs. The final fitted function for the first time



reception rate was found to follow a gamma function and an exponential function for the repeat reception rate as shown in Figure 3.3. It can be seen that the repeat reception rate was found to be constant for IDUs although the exponential function was used during sensitivity analysis (chapter 4).

Figure 3.3 - The calculated rates of (a) first time imprisonment and (b) re-imprisonment for IDUs and non-IDUs with variation in age



The complete age-specific parameter set that describes the model of the flow of IDUs through prisons in England and Wales is shown in Table 3.3.

Table 3.3 - Baseline estimates for age specific parameters

Symbol	Definition	Age Group (years)								
		15-19	20-24	25-29	30-34	35-39	40-49	50-59	60-69	70+
$\gamma (**)$	<i>Stop Rates</i>	0.0040 (*)	0.0803	0.1807	0.2796	0.3139	0.3139	0.3139	0.3139	0.3139
$\beta (**)$	<i>Start Rates</i>	0.0030	0.0045	0.0029	0.0012	0.0005	0.0001	0.0	0.0	0.0
$\rho$	<i>Discharge rates</i>	4.3574	1.9180	1.4258	1.2294	1.0063	0.9604	0.9604	0.9604	0.9604
$\rho^*$		4.5539	4.5539	4.5539	4.5539	4.5539	4.5539	4.5539	4.5539	4.5539
$\mu (**)$	<i>1st Time Imprisonment Rates</i>	0.0042	0.0018	0.0011	0.0008	0.0006	0.0004	0.0002	0.0002	0.0001
$\mu^* (**)$		0.5274	0.3144	0.2605	0.2307	0.2108	0.1905	0.1718	0.1586	0.1508
$\theta (**)$	<i>Repeat imprisonment rates</i>	1.3405	0.5778	0.2497	0.1087	0.0480	0.0163	0.0048	0.0027	0.0023
$\theta^* (**)$		0.4805	0.4805	0.4805	0.4805	0.4805	0.4805	0.4805	0.4805	0.4805

(\*) STOP RATE 0 UP TO AND INCLUDING 18 YEARS OF AGE

(\*\*) CONTINUOUS FUNCTIONS; PARAMETERS SHOWN ARE AVERAGED OVER EACH AGE GROUP

### 3.4 Discussion

This chapter considers the structure, design, and parameterisation of a model describing the flow of IDUs through prisons in England and Wales. The parameterisation described here helps to inform as to the offending behaviour of IDUs when compared to non-IDUs and their flow through prison. This model can be taken forward and applied to a range of intervention measures that target IDUs in a prison setting as will be seen in later chapters.

An alternative approach to the modelling here might be to apply a stochastic model instead of the deterministic model proposed. However the objections to this approach, are that the size of the populations under examination are quite large meaning that individual random events are unlikely to effect the model outcomes (Chapter 4, Chapter 6, and Chapter 7), while the re-parameterisation of the model that allows realistic variation in many age-specific parameters to represent the stochastic nature of the model may be problematic.

The parameter values here provide further evidence that IDUs are at increased risk of imprisonment compared to non-IDUs. However of additional interest are the discharge rates for IDUs and non-IDUs which suggest that IDUs spend less time in prison during each spell of imprisonment compared to non-IDUs. IDUs frequently commit crimes to finance their drug using habits (section 1.4) although the evidence here suggests that these crimes would appear to be relatively minor as suggested by the short estimated time spent during each spell of imprisonment.

The findings here suggest that the offending behaviour of IDUs that have previously been imprisoned is independent of age. For example the parameter estimates describing the discharge rates for IDUs suggest that IDUs are given similar length sentences independent of age, while the estimated re-imprisonment rates for IDUs are also constant across all age groups. This finding is not surprising. A current IDU here has been defined as an individual that has injected illicit drugs within the previous four weeks, and it would be expected that the criminal behaviour that these

individuals would undertake to finance their drug using habit would be independent of age.

It has been assumed here that the rate that past-IDUs restart injecting is the same as those individuals that have never injected drugs. It is acknowledged that due to relapse individuals that have previously injected drugs are more likely to start an injecting career compared to individuals that have never injected (section 1.1.1). However this assumption was made due to the paucity of data describing the rates that individuals stop and restart injecting drugs over time. Similarly it has been assumed here that IDUs start and stop injecting drugs independently of prison status, which despite evidence that prison may lead to increased likelihood of cessation and initiation of an injecting career (section 1.4) has been implemented due to paucity of data.

The model did not include the removal of individuals from each age group due to death but instead realistic age structuring was applied (Schenzle, 1984), in which all individuals within the model move up to the next age group at the end of every year and then die when reaching 75 years of age. While this solution is inevitably less realistic than applying age dependent death rates it has the advantage of maintaining an equal number of individuals within each age group, and should not impact on the results focusing on the IDU population as the majority of IDUs will have stopped injecting in the older age groups.

The model here describing the flow of IDUs and non-IDUs through prisons in England and Wales used data collected from a survey of 10 prisons undertaken in 1997 (Weild *et al.*, 2000). From this it is therefore assumed the offending characteristics of IDUs have not changed since 1997. It is acknowledged that this data is old however no further surveys have been undertaken of sufficient size that would enable the model of the flow of IDUs through prison to be re-parameterised.

The chapter here has described the parameterisation of the model describing the flow of IDUs through prisons in England and Wales. Chapter 4 takes this work forward and applies it to the HBV vaccination programme in England and Wales to show

firstly what proportion of the IDU population might be vaccinated under a range of hypothetical vaccination scenarios, and secondly to show the impact of key model parameters on model results. Chapter 7 describes an alternative application of this model considering the cost-effectiveness of HCV case-finding on reception into prisons in England and Wales.

**The research in this chapter has been published in full in the following peer reviewed article:**

**Sutton, A. J.,** Gay, N. J., Edmunds, W. J., Andrews, N. J., Hope, V. D., Gilbert, R. L., Piper, M., & Gill, O. N. (2006). Modelling the hepatitis B vaccination programme in prisons. *Epidemiol Infect.* **134**, 231-242.

## **CHAPTER 4 - MODELLING THE HEPATITIS B VACCINATION PROGRAMME IN PRISONS IN ENGLAND AND WALES**

### **4.1 Aims and introduction**

- Estimate the proportion of the IDU population in England and Wales that will become vaccinated over time under a range of realistic vaccination scenarios that describe the proportion of prisoners vaccinated on prison reception.
- Using sensitivity analysis, identify the key parameters within the model of the flow of IDUs and non-IDUs through prison (Chapter 3) that have the largest impact on estimates of the proportion of the IDU population that may become vaccinated over time.

As described in section 1.5.1.1, since June 2001 vaccination has been offered to prisoners on reception into selected prisons in England and Wales with the programme expanding to incorporate a greater number of prisons in recent years. To judge the effectiveness of the HBV vaccination programme in prisons, it is important to estimate how quickly the IDU population (which is at significant risk from HBV infection, section 1.3.1.1) will be vaccinated and the maximum proportion of IDUs that can be captured by the programme over time under a range of alternative vaccination scenarios. To address these questions the model of the flow of the IDU population through prisons described in Chapter 3 is taken forward and applied to the HBV vaccination programme in prisons in England and Wales.

The work here briefly describes how the model of the flow of IDUs through prisons is applied to the HBV vaccination programme in prisons in England and Wales. The model is then used to estimate what proportion of the total current IDU population in England and Wales will receive HBV vaccine from a range of alternative vaccination scenarios over time. Sensitivity analysis of key model parameters is also undertaken. Knowledge of what proportion of the IDU population may be vaccinated can then be

used to estimate the impact of prison vaccination on the transmission of HBV within the IDU population of England and Wales. This will be the focus of Chapter 6.

## 4.2 Methods

### 4.2.1 Model structure

The model describing the parameterisation of the flow of IDUs and non-IDUs through prisons in England and Wales has been described in Chapter 3. To apply this model to the HBV vaccination programme in prisons the vaccination status of individuals within the model must be introduced. The age-specific rates that non-IDUs and IDUs pass through prisons are estimated in Chapter 3 however the set of ordinary differential equations that describe this model are modified to include vaccination. These are described below where  $i$  is age and  $j$  is the number of doses of HBV vaccine received. Parameter definitions are described in Chapter 3:

$$\frac{dX_{ij}}{dt} = -(\mu_i + \beta_i)X_{ij} \quad 4.1$$

$$\frac{dY_{ij}}{dt} = (1 - \alpha)(X_{ij}\mu_i + Z_{ij}\theta_i) + \sum_{k=0}^3 V_{jk}(X_{ik}\mu_i + Z_{ik}\theta_i) - (\rho_i + \beta_i)Y_{ij} \quad 4.2$$

$$\frac{dZ_{ij}}{dt} = Y_{ij}\rho_i - (\theta_i + \beta_i)Z_{ij} \quad 4.3$$

$$\frac{dXI_{ij}}{dt} = \beta_i(XP_{ij} + X_{ij}) - (\mu_i^* + \gamma_i)XI_{ij} \quad 4.4$$

$$\frac{dYI_{ij}}{dt} = (1 - \alpha)(XI_{ij}\mu_i^* + ZI_{ij}\theta_i^*) + \sum_{k=0}^3 V_{jk}(XI_{ik}\mu_i^* + ZI_{ik}\theta_i^*) - (\rho_i^* + \gamma_i)YI_{ij} + \beta_i(Y_{ij} + YP_{ij}) \quad 4.5$$

$$\frac{dZI_{ij}}{dt} = \beta_i(Z_{ij} + ZP_{ij}) + YI_{ij}\rho_i^* - ZI_{ij}(\theta_i^* + \gamma_i) \quad 4.6$$

$$\frac{dXP_{ij}}{dt} = XI_{ij}\gamma_i - (\beta_i + \mu_i)XP_{ij} \quad 4.7$$

$$\frac{dYP_{ij}}{dt} = (1 - \alpha)(XP_{ij}\mu_i + ZP_{ij}\theta_i) + \sum_{k=0}^3 V_{jk}(XP_{ik}\mu_i + ZP_{ik}\theta_i) + YI_{ij}\gamma_i - (\beta_i + \rho_i)YP_{ij} \quad 4.8$$

$$\frac{dZP_{ij}}{dt} = YP_{ij}\rho_i + ZI_{ij}\gamma_i - (\theta_i + \beta_i)ZP_{ij} \quad 4.9$$

Vaccination is implemented in the model on reception into prison. A proportion  $\alpha(t)$  of prisoners entering prison are included in the vaccination programme. The



proportions of those who receive 1, 2, or 3 doses are denoted by  $a$ ,  $b$ , and  $c$  respectively. The vaccination status transition matrix  $V_{jk}$  gives the proportion of persons that had received  $k$  doses before reception into prison and  $j$  doses following reception. Where:

$$V_{jk} = \begin{pmatrix} 1-\alpha & 0 & 0 & 0 \\ \alpha a & 1-\alpha & 0 & 0 \\ \alpha b & \alpha a & 1-\alpha & 0 \\ \alpha c & \alpha(b+c) & \alpha & 1 \end{pmatrix} \quad 4.10$$

#### 4.2.2 Vaccination

Throughout the model the vaccination status of each compartment is stratified by the number of doses received, 0, 1, 2, or 3+. The prison vaccination programme is modelled by assuming 0, 1, 2, or 3 doses are administered to prisoners at the beginning of their sentence. Prison vaccine coverage (any dose) is given by parameter  $\alpha$  and is defined as the proportion of prisoners that receive at least one dose of HBV vaccine on prison reception. The parameters  $a$ ,  $b$ , and  $c$  represent the proportion of those vaccinated who receive one dose, two, or three doses of vaccine respectively ( $c=1-a-b$ ).

IDUs may be vaccinated outside prison in the community, implemented in the model as an annual event. It is assumed that a proportion  $\lambda$  of IDUs are given 3 doses and that this proportion is constant over time, with age, and with injecting career length. The model is run to steady state prior to the introduction of prison vaccination.

#### 4.2.3 Prison Vaccination

Data was collected from the HBV vaccination programme in prisons from January to June 2003 (Table 4.1) on vaccination doses administered to prisoners on reception during this period. To reduce the effects of truncation only data from March and April was considered. Excluding the other and only 4 doses received, from this data,

38% of prisoners received one dose, 28% received two doses, and 34% received three doses. This is applied to the model representing vaccination parameters a, b, and c, respectively.

**Table 4.1 - Data on HCV vaccination doses received on reception into prison during 2003 and month when first dose was administered**

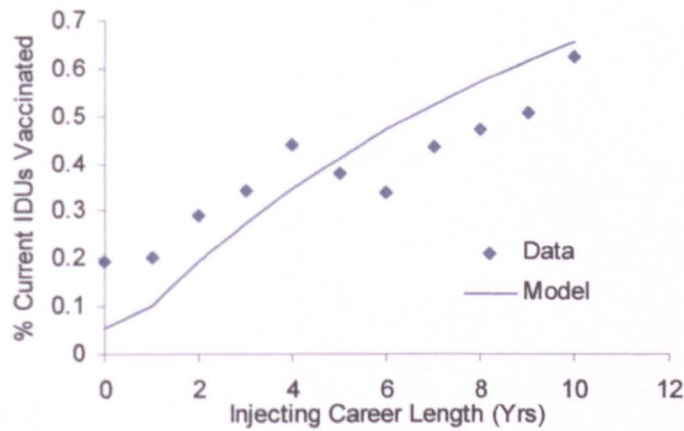
<i>Month First Dose Received</i>							
Doses							
Received	Jan	Feb	Mar	Apr	May	Jun	Total
Other	81	39	64	55	31	1	271
1&2	202	162	278	179	180	235	1236
12&3	298	400	413	275	198	54	1638
2&3	178	64	65	41	34	17	399
only 1	221	219	258	235	197	396	1526
only 2	147	53	68	74	59	101	502
only 3	383	85	85	65	83	106	807
only 4	58	105	70	76	56	74	439
Total	1568	1127	1301	1000	838	984	6818

*Reference: (Gilbert et al., 2004)*

#### 4.2.4 Community Vaccination

Data was considered from the UAPMP surveys in 2001 (Unlinked Anonymous Surveys Steering Group, 2002) of male IDUs (who injected in the previous four weeks prior to the survey) reporting whether they have been vaccinated against HBV by career length. Assuming both that this data is representative of the IDU population in the community, and that all reported vaccinations were administered in the community, the model was fitted to the data (UAPMP survey 2001) using maximum likelihood (section 3.3.3) (Figure 4.1). The proportion of IDUs vaccinated in the community ( $\lambda$ ) per year was estimated to be 0.106.

Figure 4.1 – Model fit to data describing the % of current IDUs vaccinated in 2001.



Running the model to steady state results in a fixed value of 38.4% for the proportion of IDUs vaccinated in the community in 2001 prior to the introduction of the prison vaccination programme. This compares with the 39.6% of IDUs found in the UAPMP survey 2001.

**Table 4.2 - Baseline parameter estimates and definitions.**

<i>Symbol</i>	<i>Definition</i>	<i>Baseline Value</i>
$\lambda$	The rate that IDUs are vaccinated in the community	0.106 / IDU / year
$\alpha$	The proportion of prisoners that receive at least one dose of vaccine on prison reception	Variable see text.
$a$	The proportion of those vaccinated that receive one dose of vaccine	0.38
$b$	The proportion of those vaccinated that receive two doses of vaccine	0.28
$c$	The proportion of those vaccinated that receive three doses of vaccine	0.34

### **4.3 Sensitivity Analysis**

The sensitivity analysis presented here investigates how the following factors affect the final results from the model. In each case by substituting alternative values to the baseline (parameterised in Chapter 3) as follows:

1. The total assumed size of the male IDU population inside and outside prison was chosen to be 80,000 and 160,000.
2. The average injecting career of an IDU was assumed to be 5.56 years, 6.60 years (by changing the age dependent injecting start and stop rates (Chapter 2 95% Confidence intervals)), and 20 years (assuming an age dependent start rate and constant stop rate across all ages) respectively.
3. The percentage of imprisoned young offenders that are IDUs was assumed to be 1.6% (data, section 3.3.2), 4.9%, 10% and 20%.
4. The average time an IDU spends in prison was assumed to be 2.0 months, 3.0 months, 4.0 months, 5.0 months, and 6.0 months.
5. The community vaccination rate ( $\lambda$ ) was assumed to be 0.00, 0.05, 0.075, 0.12, and 0.15 respectively.
6. To simulate the effects of a growing prison population, the 1<sup>st</sup> time and repeat reception rates into prison for IDUs and non-IDUs across all ages are assumed to increase by 1%, 2.5%, and 5% per year.

The first four factors that were tested during sensitivity analysis were used during the concurrent calculation of first time and repeat reception rates, these reception rates must be recalculated during each test of sensitivity.

As (in the base-case) the prison population size is assumed to be constant over time, i.e. the total receptions is equal to the total discharges, it is important that any changes to the model maintains this equilibrium. Thus, if for instance the % of young offenders that are IDUs is altered, then the average sentence lengths (and therefore the discharge rates) of the non-IDUs must also be adjusted.

Alongside the vaccination parameters previously described (section 4.2), the baseline vaccination scenario (section 4.3.1 below) will be used as an input into the model when testing model sensitivity.

#### 4.3.1 Vaccination Scenarios

To test the effectiveness of the HBV vaccination programme in prisons, a number of vaccination scenarios are proposed. The total proportion of prisoners on reception that participated in the HBV vaccination programme across all prisons in England and Wales during 2002 was 5%, in 2003 this figure is expected to rise to 10% and so these values are applied to all vaccination scenarios (Table 4.3). For each vaccination scenario: the parameters are at the baseline unless otherwise stated, the vaccination coverage on reception increases linearly between 2003 and 2006 where appropriate, and remains constant from 2006 onwards. In some cases the proposed vaccination scenarios are not achievable in reality (i.e. maximum scenario) however these have been selected to assist in drawing conclusions from the model.

Table 4.3 - Summary of vaccination scenarios investigated during sensitivity analysis.

Strategy	2003	2006+	Notes	Extra Strategy
Baseline	10%	50%	a = 38%, b = 28%, c = 34%	
Up to 33%	10%	33%		
Up to 66%	10%	66%		
No Expansion	10%	10%		
Targeting young offenders	10%	100%	Only young offenders are vaccinated from 2004 onwards	
Baseline + vaccination Campaign	10%	50%		Pulse: all prisoners given 3 doses at the end of 2004
Regular Campaign	10%	0%	0% vaccination on reception from 2004 onwards	Pulse: (see above) at the end of 2004, 2007, and 2010
Maximum	10%	100%	c = 100%	

## 4.4 Results

The results presented here consider the implications of various tests of sensitivity on the results obtained from the model when the baseline vaccination scenario is applied. This is followed by an examination of the potential impact of the HBV vaccination programme in prisons depending on the vaccination scenario implemented. In both cases the key result is the proportion of the IDU population both inside and outside prison that has received two or more doses of vaccine, this is considered for a number of reasons:-

1. There is some protection from infection when only one dose vaccine is administered, while a small proportion of those that receive 3 doses of vaccine may not be protected (Bock *et al.*, 1995).
2. A previous study has suggested that the 3<sup>rd</sup> HBV dose of vaccine may not be necessary (Wilson & Nokes, 1999).

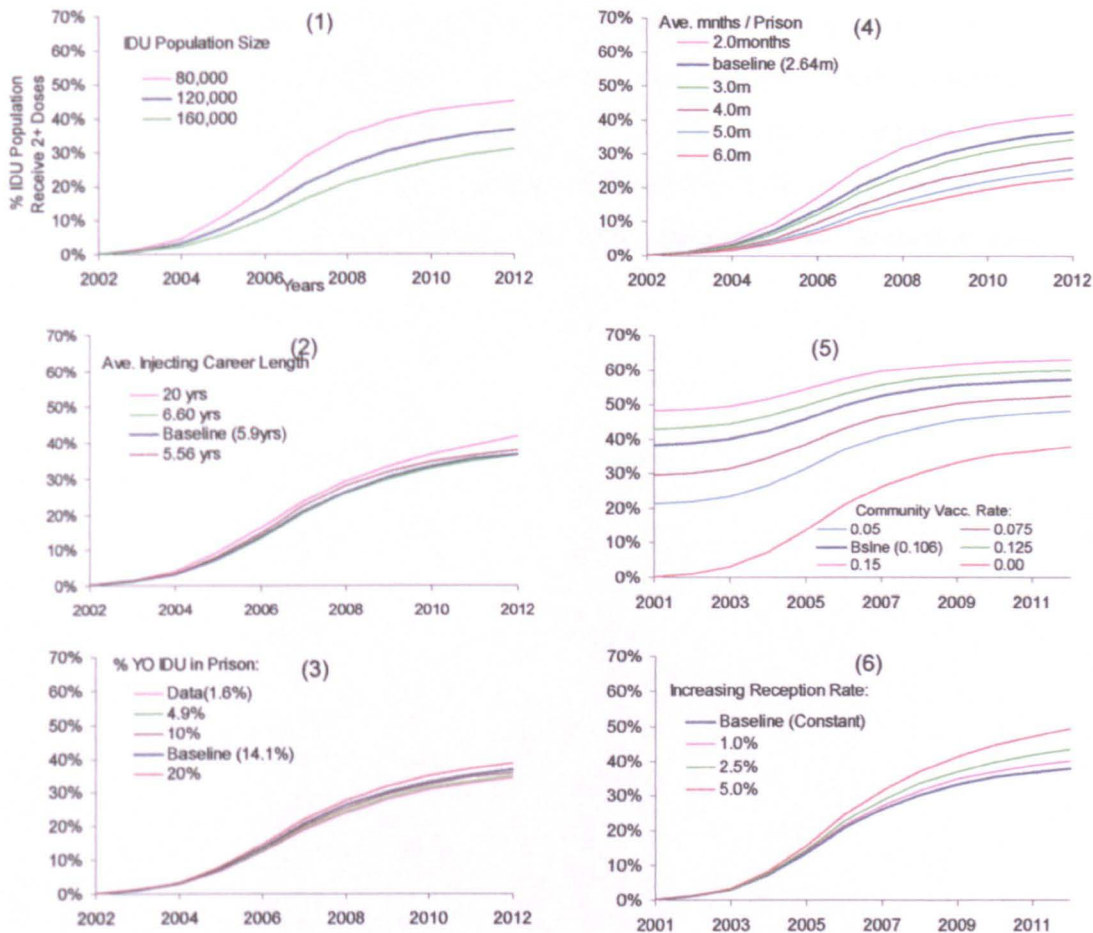
For clarity of exposition in the sensitivity analysis (excluding that examining the community vaccination rate), it has been assumed the IDU population is initially completely unvaccinated.

### 4.4.1 Results - Sensitivity Analysis

It can be seen from the results of the sensitivity analysis presented in Figure 4.2 that the factors that are most important in evaluating the success of the HBV vaccination programme in prisons are the total IDU population size, the average time that an IDU spends in prison during each prison visit, the increasing reception rate into prison over time, and the rate that IDUs are vaccinated in the community. These are the factors that contribute towards the greatest variation in results obtained from the model.



Figure 4.2 - Results of the sensitivity analysis for the prison model.



The % of the current IDU population that will have received 2+ doses of HBV over time with variations in: (1) Assumed male current IDU population size. (2) Average injecting career length. (3) % of imprisoned young offenders that are current IDUs. (4) IDU discharge rate (the average time spent in prison during each prison visit for IDUs). (5) Rate ( $\lambda$ ) that IDUs are vaccinated in the community. (6) Reception rate increase

#### 4.4.2 Results – Vaccination Scenarios

The vaccination scenarios, Baseline (50% by 2006), Up to 33% by 2006, Up to 66% by 2006 and No Expansion, all represent the potential future of the HBV vaccination programme in prisons. It can be seen (Table 4.4) that greater vaccination coverage on prison reception results in an increase in the total proportion of IDUs vaccinated (2+

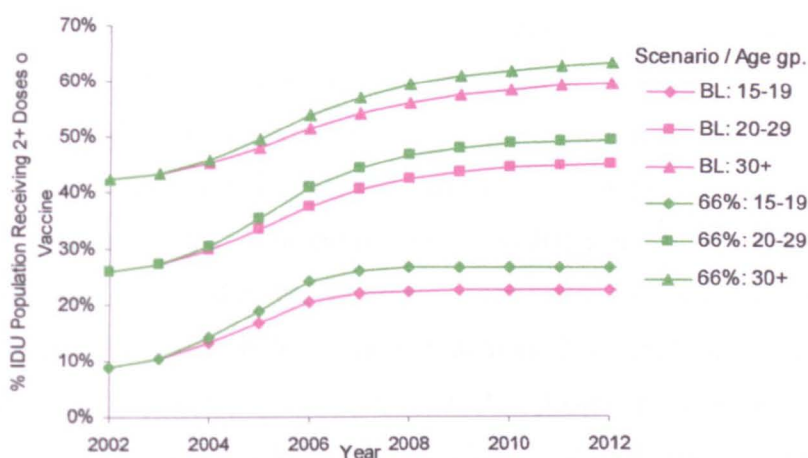
doses), an increase in the vaccination status of the prison population (2+ doses), and an increase in the number of IDUs appearing on prison reception that receive at least one dose of vaccine for the first time. However an increase in vaccination coverage on reception also requires a greater number of vaccine doses to administer the vaccination scenario. Figure 4.3 shows the vaccination status of the IDU population with variations in age when the baseline and 'up to 66% by 2006' scenarios have been applied.

Table 4.4 - Summary of results obtained from model with variations in the vaccination scenario applied.

Vaccination Scenario	Total Proportion of male prison population vaccinated		Total Proportion of male IDU population Vaccinated		Total Doses Administered	Total IDUs vaccinated for the 1 <sup>st</sup> time (*)
	By 2007	By 2012	By 2007	By 2012	By 2012	By 2012
Baseline	53.5%	66.1%	52.4%	57.2%	680,049	79,743
No Expansion	26.0%	30.0%	42.2%	43.1%	204,403	26,008
Up to 33% coverage by 2006	42.8%	53.9%	48.4%	52.1%	507,150	61,281
Up to 66% coverage by 2006	63.0%	75.6%	56.0%	61.3%	759,140	86,618
Targeting Young Offenders	33.8%	44.6%	44.6%	48.3%	298,713	24,714
Baseline + Campaign	58.8%	67.7%	53.8%	57.4%	778,096	83,000
Regular Campaign	100%	38.6%	45.6%	43.3%	425,086	17,184
Up to 100% + Campaign	99.0%	100.0%	69.4%	72.6%	1,231,559	120,392

*(\*) The number of IDUs who are completely unvaccinated on prison reception and subsequently receive at least one dose of vaccine in prison.  
Vaccinated is assumed to be those persons receiving 2+ doses of vaccine*

Figure 4.3 - The % of the IDU population that have received 2+ doses of vaccine by age.



BL = baseline, 66% = up to 66% by 2006

Assuming pessimistically that the coverage on reception does not increase from 2004 onwards, it is estimated that approximately 43% of the total IDU population will be vaccinated against HBV by 2012. This is only an additional 5% of the current IDU population being vaccinated by the prison vaccination programme, with the majority being captured by vaccination within the community. If the vaccination coverage can be increased to 66% by 2006 then this would result in an estimated 61% of the total IDU population being vaccinated by 2012. An additional 23% of the current IDU population being vaccinated in prison compared to a scenario where coverage on reception does not increase from 2004 onwards.

If from 2004 only young offenders are eligible for vaccine, and by 2006 100% of them are vaccinated on prison reception, then by 2012 approximately 48% of the IDU population are estimated to be vaccinated (2+ doses) and only approximately 24,700 IDUs would receive vaccine in prison for the first time during this period (Table 4.4). When compared to the baseline it can be seen that even if 100% of young offenders are receiving vaccination on prison reception (as is the case here), this is still less effective than expanding the vaccination coverage including all individuals (independently of age) on prison reception up to 50% by 2006.

While administering the Baseline vaccination scenario it can be seen (Table 4.4) that the introduction of an additional one-off vaccination campaign in 2004 has little long-term effect on the vaccinated IDU population. By 2012 only an additional 0.2% of IDUs would be vaccinated when compared to the Baseline scenario, this being due to the high-turnover rate of IDUs. The implementation of regular vaccination campaigns targeting the whole prison population (in this case every three years) results in a fluctuation in the proportion of IDUs and prison populations vaccinated with high values after the vaccination campaign followed by a steady decrease as vaccinated individuals leave the populations. This explains the estimated 43.3% of the IDU population and 38.6% of the prison population being captured by vaccination by 2012, a decrease from 45.6% and 100% respectively in 2007.

Increasing the vaccination coverage of prisoners on reception into prisons up to 100% by 2006, while at the same time administering a prison vaccination campaign at the end of 2004 results in 72.6% of the IDU population being vaccinated by 2012. An additional effect of this vaccination scenario is the 100% vaccinated status of the prison population. Having 100% vaccination coverage on prison reception will result in the prison population becoming completely vaccinated over time, the inclusion of the vaccination campaign results in this happening much sooner.

## **4.5 Discussion**

This chapter considers results obtained from a model of the flow of IDUs and non-IDUs through prisons applied the HBV vaccination programme in prisons in England and Wales. Sensitivity analysis of key parameters is also undertaken. Over a range of vaccination scenarios the model informs as to the effectiveness of various levels of vaccination coverage on prison reception. The model describes what proportion of the IDU population will be vaccinated over time.

Sensitivity analysis investigated the key parameters of the model of the flow of IDUs through prison that have the greatest impact on model results. The discharge rate of IDUs was found to be an important parameter that can have a significant impact on the estimated proportion of the IDU population captured by vaccine in prisons. A shorter discharge rate leads to IDUs spending less time in prisons, this means that IDUs will be released quicker and this increases the likelihood of re-imprisonment and then being re-exposed to vaccination on prison reception. The estimated size of the IDU population in England and Wales also has an impact on model results. If it is assumed that the data describing the % of the prison population that is a current IDU is correct and held constant, then a larger IDU population will result in a smaller proportion of IDUs going to prison and this leads to a reduction in the % of the IDU population that is vaccinated.

A greater community vaccination rate results in more IDUs presenting themselves on prison reception having already being vaccinated. The community vaccination rate was calculated from UAPMP data of the vaccination status of current IDUs obtained in 2001 and then for clarity of exposition the base-case scenario assumed that the community vaccination rate was constant over time from 2001 onwards. One of the problems of drawing more up to date conclusions regarding the rate that IDUs are vaccinated in the community is that more recent surveys include IDUs that have been vaccinated in prisons. As the location of vaccination is not surveyed it is difficult to tease out what the current rate of community vaccination is. However if future

surveys give information on the location of vaccination then the community vaccination rate applied here can be updated to reflect this new information.

The effectiveness of the vaccination scenario targeting only young offenders did not compare well with the vaccination scenarios advocating increased vaccination coverage of all prisoners on reception. This can be explained when considering the assumptions made during the model construction. It has been assumed due to the lack of data that persons start and stop using drugs at the same rates irrespective of prison status. Therefore persons that are currently imprisoned or have previously been imprisoned are assumed to start injecting at the same age-specific rate as those that are not. However in reality targeting young offenders for vaccination on reception into prison may lead to a greater proportion of IDUs vaccinated in the long term than has been presented here. This is because offenders, particularly young adults, are more likely to turn to drug use if they are currently in prison (Boys *et al.*, 2002) or have previously been to prison.

The results here suggest that the effect of administering a vaccination campaign either as a 'one-off' or regularly in which all prisoners currently in prison are vaccinated over a short period of time has few long-term benefits, and the focus for vaccination should be towards capturing prisoners on reception into prison. This is because the majority of IDUs pass through prison quickly (short sentence lengths) and so at the time of the vaccination campaign, relatively few IDUs will be vaccinated.

Monitoring the HBV vaccination coverage of IDUs in the community will inform as to the impact of the prison vaccination programme. This can be compared to the results from the model to see whether the predicted vaccinated status of the IDU population is comparable to actual data.

This chapter has shown that the prison vaccination programme is an effective way of improving the HBV vaccination coverage of the IDU population. Increased vaccination coverage on prison reception is preferable to a vaccination campaign in which all prisoners are vaccinated as a 'one-off', as more IDUs with shorter sentence

lengths will be captured by vaccination. Applying FOI estimates that will be estimated in Chapter 5, the impact of prison vaccination on the transmission of HBV within the IDU population will be considered in Chapter 6.

**The research in this chapter has been published in full in the following peer reviewed article:**

**Sutton, A. J.,** Gay, N. J., Edmunds, W. J., Andrews, N. J., Hope, V. D., Gilbert, R. L., Piper, M., & Gill, O. N. (2006). Modelling the hepatitis B vaccination programme in prisons. *Epidemiol Infect.* **134**, 231-242.



## **CHAPTER 5 - MODELLING THE FORCE OF INFECTION FOR HEPATITIS B AND HEPATITIS C IN INJECTING DRUG USERS IN ENGLAND AND WALES**

### **5.1 Aims and introduction**

- To estimate the FOI for HBV and HCV in IDUs in England and Wales and how this may vary over time and with injecting career length.
- To investigate the presence of heterogeneity of risk behaviour within the IDU population

A key measure of transmission within a given population is the FOI. This is defined as the instantaneous per capita rate at which susceptibles acquire infection and reflects the degree of contact with potential for transmission of infection between susceptibles and infecteds in the population (Farrington, 1990).

The aim of this chapter is to estimate FOI for HBV and HCV in the IDU population in England and Wales and how this may have evolved, both over time and as IDUs' injecting careers progress. Analysis that includes only a single infection can estimate the mean FOI but not the variance. Therefore a model is proposed here that considers HBV and HCV simultaneously and fits to observed data on the prevalence of these infections from a survey of IDUs with markers of single and multiple infections. The effects of individual heterogeneity within the IDU population are investigated, while the proposed model also considers the transmission of HBV infection in IDUs from non-IDUs. Knowledge of the risk of infection allows opportunities to apply this to models that describe the transmission of infection within a population. This can be taken forward to estimate the impact of alternative interventions on the transmission of infection. In this case the results obtained in this chapter will contribute to models that consider the transmission of HBV and HCV in the IDU population and interventions that target these infections in a prison setting (Chapter 6 and Chapter 7).

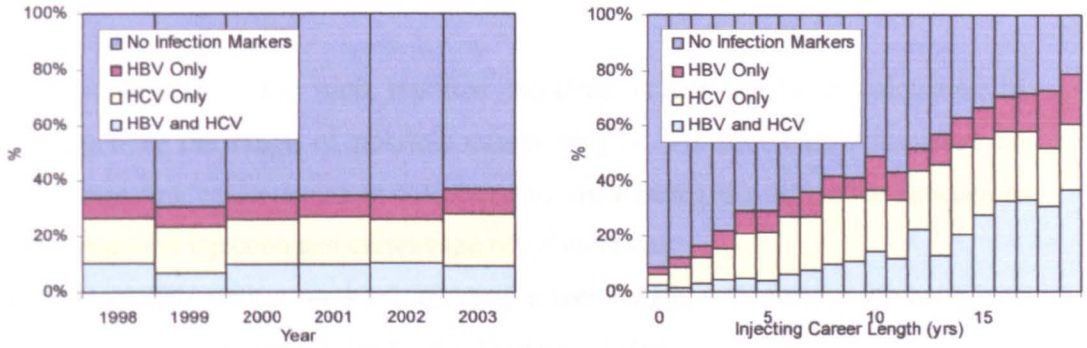
## 5.2 Methods

### 5.2.1 Data

Taking data on the IDU population of England and Wales from the UAPMP surveys as described in (section 1.2). The fields used in this analysis were: Year Surveyed, age at first injection, age when surveyed, injected in the last 4 weeks, ever vaccinated against HBV, and the number of doses of HBV vaccine received. Oral fluid samples were tested for antibody to HBV (anti-HBc) and from 1998 HCV (anti-HCV) was also included. The sensitivity and specificity of the test for anti-HBc was 75% and 100% respectively, and 83% and 100% respectively for anti-HCV (Judd *et al.*, 2003).

Throughout the thesis a current IDU is defined as having injected in the previous 4 weeks prior to being surveyed, we continue to adopt this definition here. Samples from 1990 to 1997 were not tested for HCV and so were excluded leaving six complete consecutive surveys 1998-2003 containing 12,826 records of current IDUs. Only IDUs with an unequivocal result for both tests were included in this analysis (leaving 12,814 records). The data were further constrained by limiting the current age range at the time of the survey to between 16-49 years, and the age of first injection to be from 13-45 years (12,031 records). As the FOI considers the rate that susceptibles acquire infection only those persons that were unvaccinated against HBV were considered in this analysis. (Unvaccinated IDUs were defined as those that answer no to the question of having been vaccinated against HBV and report having received no doses of HBV vaccine) (6,269 records). The percentage of the population with anti-HBc, anti-HCV, and dual infection with variation in injecting career length and over time is shown in Figure 5.1. The injecting career length for each IDU was calculated from this data by considering the difference between the current age and the age of first injecting. Due to paucity of data, those IDUs with an injecting career length of 20 years or more were omitted from this analysis, leaving 5,682 reports from IDUs to be considered here. The impact of changing this cut-off was considered during sensitivity analysis.

Figure 5.1 - The surveyed IDU population by infection status over injecting career length and time.



### 5.2.2 Force of Infection

The FOI ( $\lambda(\tau, t)$ ) may vary with time ( $t$ ) and injecting career length ( $\tau$ ). The prevalence  $P(\tau, t)$  quantifies the expected proportion of individuals with injecting career length  $\tau$  who were antibody positive at time  $t$  (Hennekens & Buring, 1987).

Prevalence in year  $t$  for those who have injected for  $\tau$  years is:

$$P(\tau, t) = 1 - e^{-\Lambda(\tau, t)} \quad 5.1$$

where  $\Lambda(\tau, t)$  is the cumulative FOI in year  $t$  for those who have injected for  $\tau$  years and is given by:

$$\Lambda(\tau, t) = \int_0^\tau \lambda(\tau', t - (\tau - \tau')) d\tau' \quad 5.2$$

this may be expressed relative to a baseline year  $T$

$$\Lambda(\tau, t) = \Lambda(\tau_0, T) + \int_{\tau_0}^\tau \lambda(\tau', t - (\tau - \tau')) d\tau' \quad 5.3$$

Where  $\tau_0 = \max(0, \tau - (t - T))$  is the career length at time T.

The cumulative FOI for each reported injecting career length is calculated by averaging over the range of possible career lengths. As previously discussed the reported injecting career length is calculated by considering the difference between an IDU's age at first injection and current age when surveyed.

Therefore an IDU with a reported injecting career length = A years, may have been injecting from (A-1) years + 1 day to (A+ 1) years – 1 day.

For those IDUs that have been injecting from (A-1) years + 1 day to A years.

The average cumulative FOI =  $\Lambda_0 + \frac{\lambda_1}{2}$  where  $\Lambda_0$  = cumulative FOI up to A-1 years and  $\lambda_1$  is the FOI from A-1 to A years.

For those IDUs that have been injecting from A years + 1 day to A+1 years – 1 day the average cumulative FOI =  $\Lambda_0 + \lambda_1 + \frac{\lambda_2}{2}$  where  $\lambda_2$  is the FOI from A to A+1 years.

Therefore the average cumulative FOI experienced by IDUs reporting an injecting career length of A is

$$\Lambda_0 + \frac{3\lambda_1}{4} + \frac{\lambda_2}{4} \quad 5.4$$

### 5.2.3 Model

The status of each IDU is considered with respect to both infections. To introduce individual heterogeneity of at-risk behaviour into the model we introduce a frailty Z which represents an individual's relative rate of infection. An individual of frailty Z and career length  $\tau$  at time t has the risk  $1 - e^{-Z\Lambda_B(\tau,t)}$  of previous HBV infection and  $1 - e^{-Z\Lambda_C(\tau,t)}$  of previous HCV infection. The frailty distribution is assumed gamma with shape  $\theta$  and scale parameter = 1.

For infection acquired through injecting drug use only, let  $\pi_{00}(\tau,t)$ ,  $\pi_{B0}(\tau,t)$ ,  $\pi_{0C}(\tau,t)$  and  $\pi_{BC}(\tau,t)$  denote the proportion of IDUs in year t with an injecting

career length of  $\tau$  that are uninfected, infected by HBV not HCV, infected by HCV not HBV, and both HBV and HCV respectively.

Beginning with the following equations proposed by (Farrington *et al.*, 2001).

$$\pi_{00}(\tau, t) = \left\{ 1 + \frac{Y_B(\tau, t) + Y_C(\tau, t)}{\theta} \right\}^{-\theta} \quad 5.5$$

$$\pi_{B0}(\tau, t) = \left\{ 1 + \frac{Y_C(\tau, t)}{\theta} \right\}^{-\theta} - \pi_{00}(\tau, t) \quad 5.6$$

$$\pi_{0C}(\tau, t) = \left\{ 1 + \frac{Y_B(\tau, t)}{\theta} \right\}^{-\theta} - \pi_{00}(\tau, t) \quad 5.7$$

$$\pi_{BC}(\tau, t) = 1 - \pi_{B0}(\tau, t) - \pi_{0C}(\tau, t) - \pi_{00}(\tau, t) \quad 5.8$$

The variables  $Y_B$  and  $Y_C$  should not be interpreted as the cumulative FOI for HBV and HCV respectively because the total prevalence of each infection depends on  $\theta$ . We re-parameterize these equations so that the total prevalence of each infection is independent of  $\theta$  as shown below.

We define

$$\Lambda_b = \theta \text{Ln} \left\{ 1 + \frac{Y_B}{\theta} \right\} \quad 5.9$$

and

$$\Lambda_c = \theta \text{Ln} \left\{ 1 + \frac{Y_C}{\theta} \right\} \quad 5.10$$

These are then substituted into Farrington's equations above giving:

$$\pi_{00}(\tau, t) = (e^{\frac{\Lambda_b(\tau, t)}{\theta}} + e^{\frac{\Lambda_c(\tau, t)}{\theta}} - 1)^{-\theta} \quad 5.11$$

$$\pi_{B0}(\tau, t) = e^{-\Lambda_c(\tau, t)} - \pi_{00}(\tau, t) \quad 5.12$$

$$\pi_{0C}(\tau, t) = e^{-\Lambda_b(\tau, t)} - \pi_{00}(\tau, t) \quad 5.13$$

$$\pi_{BC}(\tau, t) = 1 - \pi_{00}(\tau, t) - \pi_{B0}(\tau, t) - \pi_{0C}(\tau, t) \quad 5.14$$

where:

$$\text{Total prevalence of HBV} = \pi_{B0} + \pi_{BC} = 1 - e^{-\Lambda_B} \quad 5.15$$

$$\text{Total prevalence of HCV} = \pi_{C0} + \pi_{BC} = 1 - e^{-\Lambda_C} \quad 5.16$$

And therefore:

$\Lambda_B(\tau, t)$  and  $\Lambda_C(\tau, t)$  are the cumulative FOI for HBV and HCV respectively in year  $t$  for injecting career length  $\tau$ .

#### 5.2.4 HBV Background Prevalence and Test Sensitivity

Background HBV prevalence is included in the model and reflects the possibility of transmission of HBV from outside the IDU population. As 95% of reports with exposure data to HCV indicate injecting drug use (Health Protection Agency *et al.*, 2005), it has been assumed here that there was no non-injecting related transmission of HCV. To incorporate HBV background prevalence and the sensitivity of the HBV and HCV tests into this model the equations describing the prevalence of the two viruses  $\pi_{xy}(\tau, t)$  have been modified to both reflect the possibility that HBV infection can occur for reasons other than injecting and that the tests for HBV and HCV have a sensitivity and specificity that is less than 100%. It is assumed in this model that the risk of background HBV infection is constant through time and injecting career length.

$$P_{0y} = \pi_{0y}(1 - b) \quad 5.17$$

$$P_{By} = \pi_{By} + \pi_{0y}b \quad 5.18$$

and

$$V_{00} = P_{00} + (1 - s_B)P_{B0} + (1 - s_C)P_{0C} + (1 - s_B)(1 - s_C)P_{BC} \quad 5.19$$

$$V_{B0} = P_{B0}s_B + s_B(1 - s_C)P_{BC} \quad 5.20$$

$$V_{0C} = P_{0C}s_C + s_C(1 - s_B)P_{BC} \quad 5.21$$

$$V_{BC} = s_B s_C P_{BC} \quad 5.22$$

where

$b$  = background prevalence of infection of HBV.

$s_B$  = sensitivity of the HBV test

$s_C$  = sensitivity of the HCV test

$P_{xy}$  = proportion of IDUs in year  $t$  with an injecting career length of  $\tau$  with status  $xy$  allowing for the background prevalence of infection of HBV .

$V_{xy}$  = proportion of IDUs in year  $t$  with an injecting career length of  $\tau$  who have test status  $xy$  (allowing for the sensitivity of the HBV and HCV tests)

#### 5.2.5 Parameterisation

The cumulative FOI in 1998 (the first year of data considered here for each virus) by injecting career length,  $\Lambda(1998, \tau)$  is described by the function  $f(\tau)$ . This is described by a four parameter logistic function.

$$f(\tau) = z + \frac{(u - z)}{1 + (e^{(r-w)})^v} \quad 5.23$$

The cumulative FOI in 1998 describes all infection in previous years and is estimated with the FOI for the more recent years (1999-2003). No attempt has been made to reduce the parameters describing this function with the priority being to ensure sufficient flexibility and a good fit to the data.

The FOI from 1999 onwards is modelled as the product of a function describing its trend over time  $g(t)$  and a function describing its trend with injecting career length  $h(\tau)$  (Ades & Nokes, 1993):

$$\lambda(t, \tau) = g(t)h(\tau) \quad 5.24$$

To standardize results for each virus,  $h(0)$  is fixed equal to 1. Both  $g(t)$  and  $h(\tau)$  are parameterized on piecewise constant functions

The initial model used at the start of the analysis is defined as describing function  $f(\tau)$  for each virus with a four parameter logistic function (8 parameters), and functions  $g(t)$  and  $h(\tau)$  for each virus are described by an individual value for each year 1999-2003 (10 parameters) and injecting career length 1-19 years respectively (38 parameters). Along with the parameters frailty  $\theta$  and HBV background prevalence  $b$ , this leads to the initial model being described by 58 parameters.

It is assumed that IDUs who report an injecting career length of 0 years have been injecting for an average of 6 months (section 5.2.2). IDUs who appear in the UAPMP surveys such as those considered here, are recruited from those in contact with services. The probability of being in contact with services increases with injecting career length (Chapter 2) and therefore the average career length of surveyed new initiates may be higher than the 6 months assumed. Because the estimated FOI in new initiates will be correlated with the duration of exposure (injecting career length) we investigate the sensitivity of our estimates to the career length assumed. As an extreme case, it is assumed that IDUs with a reported injecting career length of 0 years have been injecting for 12 months, while applying the injecting career length of the remaining IDUs at reported levels.

### 5.2.6 Model Fitting

If  $n_{xy}(\tau, t)$  denotes the number of individuals in year  $t$  with injecting career length  $\tau$  with test results coded  $xy$  as above, the log-likelihood ( $L$ ) is the product multinomial.

$$L = \sum_t \sum_x \sum_{\tau=0}^I n_{xy}(\tau, t) \log \{V_{xy}(\tau, t)\} \quad 5.25$$



Beginning with an initial model and then maintaining the four parameter logistic function for  $f(\tau)$ , backwards-stepwise elimination was used to reduce the number of parameters describing  $g(t)$  and  $h(\tau)$ . Models were compared using the analysis of deviance with the Chi-squared test, the criteria for dropping parameters being that  $p > 0.05$ . When the parsimonious model (the best fitting model with the fewest parameters) had been identified, CIs were calculated using profile likelihood. For both functions  $g(t)$  and  $h(\tau)$  a range of alternative reduced models were considered including alternative values for the fixed category of  $h(0)$  e.g. 0 years 0-1 years, 0-2 years etc. A selection of the reduced models examined during the backwards-stepwise elimination process is described in the following (only changes from the initial model are noted):

1. Initial model
- 2  $h(\tau)$  for each virus is grouped into 4 injecting career length groups (1-2 yrs, 3-4yrs, 5-9yrs, 10+yrs, 0yrs is fixed)
- 3 As model 2 above, except  $h(\tau)$  is the same for each virus.
- 4 As model 3 above, except  $h(\tau)$  is described by 1 injecting career length group (1+ years, 0yrs is fixed)
- 5 As model 4 above, except  $g(t)$  for each virus is a single parameter (1999-2003).
- 6 As model 5 above, except function  $h(\tau) = 1$ .

### 5.3 Results

The calculated model parameters for the parsimonious model are shown in Table 5.2 with 95% CIs. The results from the model suggest that HBV background prevalence is low ( $=0.00$ , 95% CI: 0-0.0161).

Table 5.1 shows a summary of the results of the fitting procedure. The initial model gave a good fit to the data and successive reducing in the number of parameters in models 2-5 did not significantly worsen the fit. Model 6 considered the impact of removing the function  $h(\tau)$ , however this provided a significantly less good fit than Model 5 ( $p < 0.001$ ). Model 5, therefore, was taken to be the parsimonious model.

Table 5.1 - Goodness of fit for initial and reduced models

Model	d.f. (n=471)	Deviance	p value
1 (Initial Model)	413	392.2	
2	443	413.6	0.87
3	447	415.6	0.73
4	450	417.9	0.52
5	458	428.8	0.21
6	459	469.6	<0.0001

Table 5.2 - Parameter values describing the parsimonious model

Parameter	HBV	95% CI	HCV	95% CI	Global	95% CI
g(t) trend in the FOI by year 1999-2003	0.1079	(0.0840-0.1327)	0.1608	(0.1314-0.1942)		
h( $\tau$ ) trend in the FOI by injecting career length						
<1	1	Fixed	Same as HBV			
1+	0.3272	(0.2359-0.4443)	Same as HBV			
HBV background prevalence					0	(0.0-0.0161)
Frailty $\theta$					0.6566	(0.5305-0.8224)
	u	-0.132	-2.524			
	v	0.117	0.026			
	w	63.99	77.52			
	z	295.5	19.49			

Figure 5.2 shows the estimated FOI by injecting career length for HBV and HCV, while the model fit to data for each survey is shown in Figure 5.3. Across similar injecting career lengths the FOI was found to be higher for HCV than HBV. For both HBV and HCV the FOI is higher for new initiates to injecting (injecting career length <1 year) (Figure 5.2) compared to experienced IDUs.

Figure 5.2 - The FOI for HBV and HCV with variation in injecting career length for 1999-2003.

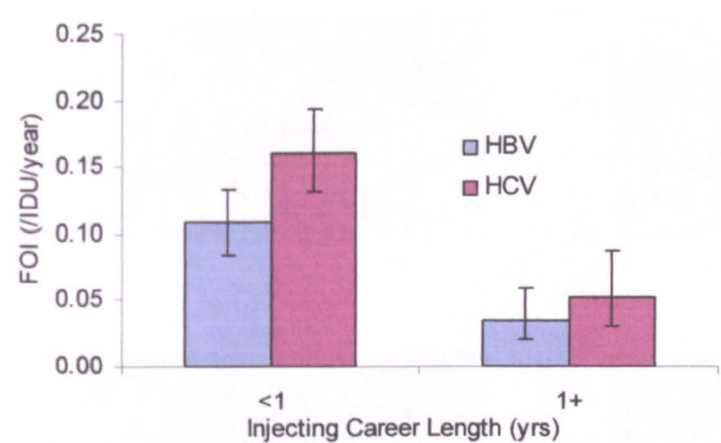
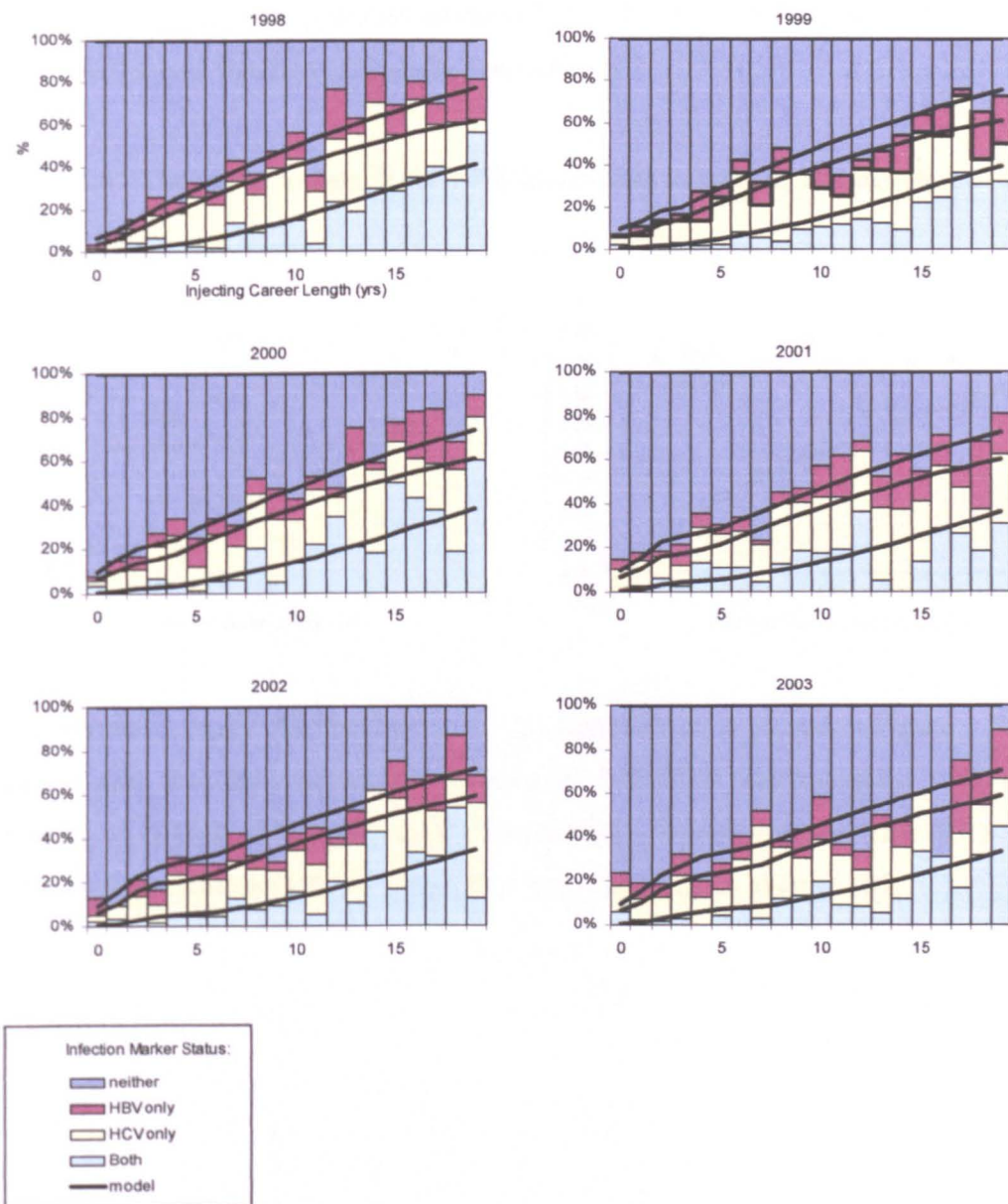
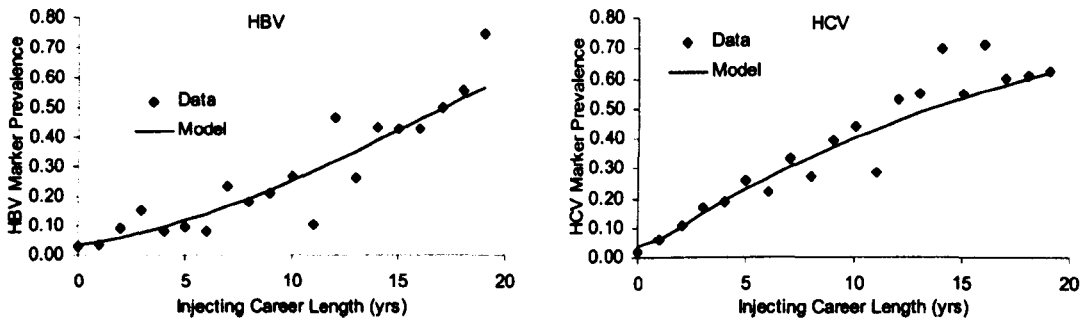


Figure 5.3 - Model fit to data for each survey 1998-2003



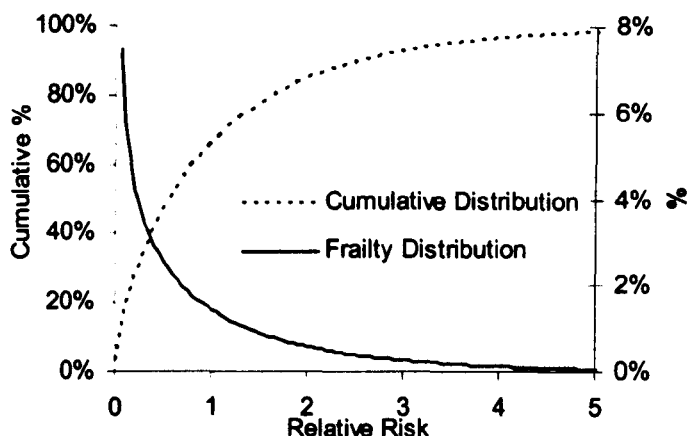
The model fit to data for HCV and HBV in 1998 is shown in Figure 5.4. The close fit of the model to the data provides additional confidence in the selection of the four parameter logistic function to describe function  $f(\tau)$ .

Figure 5.4 - The model to data fit for 1998 survey data describing the prevalence of HBV and HCV infection.



The estimated frailty distribution for the IDU population is shown in Figure 5.5. It can be seen that there is strong evidence of individual heterogeneity, with the majority of IDUs (64%) having a FOI less than the average (relative risk (RR)<1), and a small proportion (15%) having a FOI much higher than average (RR >2).

Figure 5.5 - The estimated frailty distribution and a cumulative density function describing the frailty for HBV and HCV.



To investigate the impact of excluding those IDUs with an injecting career length of 20 years or greater, a further reduction was made with IDUs with an injecting career length of greater than 10 years being excluded from the analysis. However model results were found to be similar (Table 5.3) thereby suggesting no good reason to further reduce the number of IDUs included in this analysis.

Table 5.3 - FOI estimates for HBV and HCV with variations in injecting career length.

		Injecting career <1 years	1+ Years
length			
HBV	0-10 years	0.1079 (95% CI: 0.0805-0.1347)	0.0349 (0.0185-0.0586)
	<20 years	0.1079 (0.0840-0.1327)	0.0353 (0.0198-0.0590)
HCV	0 -10 years	0.1644 (0.1339-0.1989)	0.0531 (0.0307-0.0865)
	<20 years	0.1608 (0.1314-0.1942)	0.0526 (0.0310-0.0863)

*When IDUs with an injecting career length of greater than 10 years are excluded from the analysis compared to the baseline that includes IDUs with an injecting career length less than 20 years.*

The importance of considering the test sensitivity for HBV and HCV in the model was shown when these are excluded from the model. The resultant FOI estimates for both HBV and HCV were found to be lower than when test sensitivity is included in the model (Table 5.4).

**Table 5.4 - The impact of the exclusion of the test sensitivities on the FOI estimates for HBV and HCV.**

Test Sensitivity		<1 years	1+ Years
HBV	Excluded	0.0807 (95% CI: 0.0640-0.0992)	0.0253 (0.0147-0.0383)
	Included	0.1079 (0.0840-0.1327)	0.0353 (0.0198-0.0590)
HCV	Excluded	0.1313 (0.1082-0.1582)	0.0411 (0.0247-0.0611)
	Included	0.1608 (0.1314-0.1942)	0.0526 (0.0310-0.0863)

It has been assumed that all new initiates to injecting (injecting career length=0yrs) have been injecting for an average six months. However if instead it is assumed that all IDUs in the surveys have been injecting for at least 1 year, then this lessens (but does not remove) some of the injecting career length effect on the FOI ( $h(1+)=0.5704$ , 95% CI: 0.4471-0.7801) although as before the strong evidence of individual heterogeneity remains ( $\theta = 0.6547$ , 95% CI: 0.5301-0.8208).



## 5.4 Discussion

UAPMP data collected from IDUs in England and Wales (section 1.2) was analysed to estimate the trend in the FOI for HBV and HCV in IDUs over time and career length. By considering both viruses together we assessed the heterogeneity of risk within the IDU population and the effect of background HBV transmission due to transmission between IDUs and non-IDUs.

As has been discussed in section 1.1 IDUs recruited into surveys such as the UAPMP surveys considered here may not be representative of the whole IDU population. For example if there is a greater difference in HCV prevalence among new initiates contacting and not contacting services than among experienced IDUs, then this will influence the estimated difference in FOI between new and experienced IDUs compared to the actual FOI in the overall IDU population. It has been assumed that the risk behaviour in the surveyed IDU population considered here is the same as the IDU population in England and Wales and additionally it is assumed there is the same likelihood of a positive or negative IDU being surveyed as there would be in the IDU population in England and Wales. These assumptions are typically difficult to corroborate as it is hard to imagine future surveys of IDUs that are not biased towards more experienced IDUs, as new initiates will always be more difficult to recruit into surveys of current IDUs (section 1.2).

The model suggests that the FOI of HBV and HCV is up to four times higher among new initiates (injecting career length <1 year) than for IDUs with longer injecting careers, a finding which is supported by previous studies (Kretzschmar & Wiessing, 2004; Rothenberg *et al.*, 1998). In all cases it was found that there is increased risk of infection in new initiates compared to experienced IDUs. The scale of these findings must be approached with caution as they are sensitive and dependent on information about and from a small sub-group of IDUs (those with injecting career lengths of less than 1 year). It has been assumed that IDUs reporting an injecting career length of 0 years (i.e. start age = current age), have an even chance of their exact injecting career length being anything from 0 days to 1 year. However this does not allow for the

delay from the initiation of injecting until coming into contact with services. If it is assumed instead that all current IDUs (including new initiates) in the surveys have been injecting for at least one year, the injecting career length effects are lessened with new initiates only having FOI estimates for HBV and HCV up to twice as high as experienced IDUs.

The model indicates considerable heterogeneity in the FOI among the sample suggesting some IDUs are at significantly greater risk from infection from BBVs within the larger IDU population. Analysis that considers only a single infection cannot address the issue of individual heterogeneity, or its effect on other estimates. In such analysis the presence of high risk individuals within the IDU population would cause an apparently higher FOI in IDUs with short injecting career lengths. However such a career length effect is found here after allowing for individual heterogeneity. These results demonstrate the added value of this combined analysis. From this data alone it is impossible to draw any conclusions about the reasons for this individual heterogeneity, although it could be due to certain groups within the overall IDU population stratified by ethnicity, socioeconomic status, sex, or other demographic variables.

It is acknowledged that the prevalence of each virus within the IDU population may be due to infection from outside the IDU population particularly for HBV. However the low prevalence of background HBV infection suggests that the infection in the IDU population is primarily due to contact between IDUs (needle sharing or sexual contact).

One of the key assumptions in the proposed model is how long a new initiate to injecting (injecting career length =0 years) has actually been injecting. It has been assumed at baseline that a new initiate has been injecting for six months which is half way between the possible injecting career lengths (0days – 364days) of an IDU that reports an injecting career length of 0 years. The impact of varying this assumption is that the assumed time that a new initiate is at risk from injecting related infection will either be increased or decreased. This has a significant impact on model results, with

variation in the trend in the FOI over injecting career length being dependent on this assumption.

During this analysis we excluded those IDUs that reported being vaccinated against HBV. This was done as their inclusion would result in an underestimation in the FOI estimates obtained for HBV. When individuals are diagnosed with HCV infection, due to complications associated with dual infection they should be vaccinated against HBV (Salisbury & Begg, 1996). A consequence of this is that some individuals that are HCV positive and vaccinated against HBV were excluded from this analysis. As the prevalence of HCV is higher in those IDUs that are excluded from this analysis (vaccinated against HBV) compared to those included (RR=1.15, 95% CI: 1.09-1.21 adjusting for injecting career length), the results here may underestimate the FOI in IDUs for HCV. To overcome this and to allow a greater number of IDUs to be included in the analysis, future models should incorporate an HBV vaccination rate that varies based on IDUs' HCV status, this will lead to a greater number of IDUs being included in this analysis (vaccinated and unvaccinated) and may help to remove any bias in the FOI estimates obtained here. An additional advantage of this is that an increase in the number of HCV positive individuals included in this analysis may also increase power to detect any changes in the FOI over time.

The estimation of the FOI from serial prevalence data provides added epidemiological value. Previous authors have studied the incidence of infection in a cohort of IDUs (Judd *et al.*, 2005) although to the authors' knowledge no previous studies have used this method of modelling to estimate the FOI for HBV and HCV in the IDU population. The models highlight the need to increase interventions that target new initiates to injecting to reduce the transmission of BBVs. Although from the evidence here, identification of those individuals that engage in heightened at-risk behaviour should be undertaken. The data and methods described here may provide a baseline for monitoring the success of public health interventions.

This chapter concludes work examining the rate that susceptible IDUs acquire infection from HBV and HCV. This work is taken forward and used to parameterise a model describing the transmission of HBV within the IDU population and the cost-

effectiveness of HCV case-finding on prison reception. This will be the focus of Chapter 6 and Chapter 7 respectively.

**The research in this chapter has been published in full in the following peer reviewed article:**

**Sutton, A. J., Gay, N. J., Edmunds, W. J., Hope, V. D., Gill, O. N., & Hickman, M. (2006). Modelling the force of infection for hepatitis B and hepatitis C in injecting drug users in England and Wales. *BMC Infect.Dis.* 6, 93.**

## **CHAPTER 6 - MODELLING THE IMPACT OF THE HEPATITIS B PRISON VACCINATION PROGRAMME ON HEPATITIS B TRANSMISSION WITHIN THE INJECTING DRUG USER POPULATION OF ENGLAND AND WALES**

### **6.1 Aims and introduction**

- To parameterise a model describing the transmission of HBV within the IDU population of England and Wales.
- To investigate the impact of HBV vaccination on reception into prisons in England and Wales on the incidence and prevalence of HBV within the IDU population of England and Wales.
- To conduct sensitivity analysis of key parameters within the proposed transmission model.

Chapter 3 describes a model of the flow of IDUs and non-IDUs as they pass through prisons in England and Wales. In Chapter 4 this model is applied to show the potential coverage of the HBV vaccination programme in prisons in England and Wales. This work demonstrated that over a range of vaccination scenarios, 57% of the IDU population might be vaccinated by 2012 if coverage of 50% or more on prison reception could be achieved across all prisons in England and Wales. However this model does not show the impact that this vaccination programme may have on the transmission of HBV within the IDU population in England and Wales.

The model proposed here describes the dynamics of HBV transmission in the IDU population of England and Wales. The work here takes estimates of the proportion of the IDU population vaccinated from the model of the HBV vaccination programme in prisons (Chapter 4) under a range of vaccination scenarios and considers the effect of this programme on the incidence and prevalence of HBV in the IDU population in England and Wales. Sensitivity analysis of the key model assumptions and parameters is undertaken.

## 6.2 Methods

The model presented here considers the transmission of HBV due to contact between IDUs. This represents the sharing of injecting paraphernalia and other at-risk practices that may lead to the transmission of BBVs; this may also include the potential for transmission via sexual contact between IDUs.

### 6.2.1 Model Structure

Only the IDU population of England and Wales is considered with non-IDUs being excluded from this analysis, and it is assumed that the IDU population is of fixed size and equal to 160,000 (Frischer *et al.*, 2001) (section 1.1.1). The results from the model of the HBV vaccination programme in prisons in England and Wales have been used here (Chapter 4), and as this model considers only males, it has been assumed here that female IDUs have the same offending characteristics as males.

Using a mathematical model of HBV natural history and transmission dynamics (Medley *et al.*, 2001; Edmunds *et al.*, 1996a; Williams *et al.*, 1996), the IDU population is stratified into six epidemiological groups: those who are susceptible to infection, denoted S; those who have been infected but are not yet infectious, L; acute infections, A, who are in the initial highly infectious stage of infection; those who are carriers, C; vaccinated, V, those that have been vaccinated and are immune from infection; and those with protective immunity, R, due to recovery from either carrier or acute stages of infection. As the model includes an injecting career length dependent FOI the IDU population is stratified by injecting career length.

IDUs enter the model at the start of the year into the first injecting career length cohort. Thereafter individuals change cohorts at the beginning of each year. The rates, with respect to both injecting career length and time, at which individuals flow from one epidemiological state to another, are described by a system of differential equations.

The differential equations for the deterministic model are as follows:

$$\frac{dS_0}{dt} = \alpha - \mu_0 S_0 - \lambda_0(t) S_0 - v_0(t) S_0 \quad 6.1$$

$$\frac{dS_i}{dt} = -\mu_i S_i - \lambda_i(t) S_i - v_i(t) S_i \text{ where } i = 1, 2, 3 \text{ etc.} \quad 6.2$$

$$\frac{dL_i}{dt} = \lambda_i(t) S_i - \mu_i L_i - \sigma L_i \quad 6.3$$

$$\frac{dA_i}{dt} = \sigma L_i - \mu_i A_i - \gamma_1 A_i \quad 6.4$$

$$\frac{dC_i}{dt} = p \gamma_1 A_i - \mu_i C_i - \gamma_2 C_i \quad 6.5$$

$$\frac{dR_i}{dt} = (1 - p) \gamma_1 A_i + \gamma_2 C_i - \mu_i R_i \quad 6.6$$

$$\frac{dV_i}{dt} = v_i(t) S_i - \mu_i V_i \quad 6.7$$

where  $i$  represents the injecting career length class,  $\sigma$  represents the rate at which the latently infected become infectious, and  $\gamma_1$  and  $\gamma_2$  are the recovery rates of acute infections and carriers, respectively. (Note that  $1/\sigma$ ,  $1/\gamma_1$  and  $1/\gamma_2$  are, respectively, the average duration of the latent, acute and carrier states.) The number of new IDUs that start injecting each year is represented by  $\alpha$ . The probability that an individual fails to clear an acute infection and develops the carrier state is represented by  $p$ .

The rate at which individuals with injecting career length  $i$  leave the IDU population is denoted  $\mu_i$  (dependent of injecting career length and time). The vaccination rate is denoted as  $v_i(t)$ . The FOI  $\lambda_i(t)$ , also depends on injecting career length and time. The FOI acting on susceptibles with an injecting career length of  $i$  at time  $t$  is assumed to be

$$\lambda_i(t) = \sum_{j=0}^{j=\rho} \beta_{ij} [A(t)_j + \delta C(t)_j] \quad 6.8$$

where  $\beta_{ij}$  describes the transmission coefficient between susceptibles of injecting career length  $i$  and infectious individuals (both carriers and acute infections) of injecting career length  $j$ , and  $\delta$  represents the relative infectiousness of carriers compared with acute infections (Edmunds *et al.*, 1996a) and  $\rho$  is the number of injecting career length classes. The initial conditions  $X_i(\cdot)$ ,  $L_i(\cdot)$ ,  $A_i(\cdot)$ ,  $C_i(\cdot)$ ,  $R_i(\cdot)$ , and  $V_i(\cdot)$  are the numbers of IDUs of injecting career length  $i$ , in each state at time=0 and are taken to be the equilibrium number of susceptibles, latents, acutes, carriers, immunes, and vaccinated prior to the introduction of prison vaccination (but with community vaccination). This was found by setting the time derivatives to zero and solving the resulting set of simultaneous equations to yield the equilibrium numbers of susceptibles, latents and so on.

## 6.2.2 Parameterisation

### 6.2.2.1 IDU Population Data

It has been assumed that an IDU has an average injecting career length of 5.97 years. This estimate is taken from Chapter 2 coupled with the fixed IDU population size of 160,000 this leads to  $\alpha=26,801$  IDUs starting injecting each year. The removal rates are defined as the rates that IDUs leave the IDU population due to either the cessation of injecting or death. Assuming that the age dependent removal rates provided in Chapter 2 are a reasonable approximation of the rate at which IDUs leave the IDU population, to be compatible with the model presented here, these removal rates are converted to be injecting career length dependent.



### 6.2.2.1.1 Removal Rates

The age-specific removal rates are converted to be injecting career length specific via the following method:

$n_{ki}$  is defined as the total number of IDUs with injecting career length  $i$  of age  $k$  and is equal to

$$n_{ki} = \alpha f_{k-i} \prod_{j=0}^{i-1} (1 - \omega_{k-j}) \quad 6.9$$

where  $f_k$  is the proportion of IDUs starting injecting at age  $k$ , and  $\omega_k$  is the age dependent stop rate

The total number of IDUs with an injecting career length  $i$ ,  $N_i$  is

$$N_i = \sum_{k=15}^{k=75} n_{ki} \quad 6.10$$

and

$$\mu_i = -\ln \frac{N_i}{N_{i+1}} \quad 6.11$$

### 6.2.2.2 The force of infection and transmission coefficients

The FOI estimates presented here are taken from Chapter 5 which considered the IDU population as being divided into two groups which have been adopted here; new initiates, i.e. those injectors with an injecting career length of less than 1 year, and experienced IDUs, i.e. those injectors with an injecting career length of greater than 1 year. It was found that the FOI for HBV had not changed from 1999-2003 and so it is assumed here that the FOI is constant within both of the discrete injecting career length groups prior to the introduction of prison vaccination.

As the FOI is different for new initiates to injecting (injecting career length <1year) and experienced IDUs (injecting career length 1+ years), the FOI within each of these discrete injecting career length groups is described by the following 2 equations:

$$\lambda_1 = \beta_{11} \sum_{i=0}^{i=1} (A_i + \delta C_i) + \beta_{12} \sum_{i=1}^{i=\infty} (A_i + \delta C_i) \quad 6.12$$

$$\lambda_2 = \beta_{21} \sum_{i=0}^{i=1} (A_i + \delta C_i) + \beta_{22} \sum_{i=1}^{i=\infty} (A_i + \delta C_i) \quad 6.13$$

where

$\lambda_1$  is the FOI for those IDUs with an injecting career length of <1 years.

$\lambda_2$  is the FOI for those IDUs with an injecting career length of 1+ years.

The transmission coefficients,  $\beta_{mn}$ , are the per capita rate of effective contact between two IDUs of career length m and n (where an index = 1 represents those with an injecting career length of less than 1 year, and 2 those with a career length of more than 1 year). They were calculated from the equilibrium values of  $\lambda_n$  the FOI for individuals in group n and the number of carriers and acutes in the population at steady state assuming proportional mixing. This type of mixing arises when individuals make contacts with other people in their own or other groups in proportion to the number of contacts that are supplied from each group (Garnett *et al.*, 1992).

#### 6.2.2.2.1 Proportional Mixing

For proportional mixing  $\beta_{ij}$  is defined as:

$$\beta_{ij} = \frac{d_i d_j N_j}{d_i N_i + d_j N_j} \quad 6.14$$

Where  $d_i$  is the effective contact rate for individuals in group  $i$ , and  $N_i$  is the number of individuals in group  $i$ .

The estimates of the transmission coefficients for the 'Who acquires infection from whom' (WAIFM) matrix are shown in Table 6.1:

Table 6.1 - The structure of the WAIFM matrix ( $\beta_{ij}$ ) with values at baseline.

	j=1	2
i=1	$1.69 \cdot 10^{-4}$	$5.53 \cdot 10^{-5}$
2	$5.53 \cdot 10^{-5}$	$1.81 \cdot 10^{-5}$

*The injecting career length groups (numbered 1 to 2) refer to <1 years, and 1+ years respectively.*

A summary of parameters is given in Table 6.2 along with a reference to the data source as appropriate.

Table 6.2 - Baseline parameter estimates used in numerical simulations

<i>Parameter</i>	<i>Symbol</i>	<i>Value</i>	<i>Data Sources</i>
FOI in new initiates prior to the introduction of prison vaccination	$\lambda_1$	0.1079 per year,	Chapter 5
FOI in experienced IDUs prior to the introduction of prison vaccination	$\lambda_2$	0.0353 per year,	Chapter 5
IDU population size		160,000	Frischer <i>et al.</i> , (2001)
Rate of lose of latency	$\sigma$	6 per year	Edmunds <i>et al.</i> , (1996a)
Recovery rate (acutes)	$\gamma_1$	4 per year	Edmunds <i>et al.</i> , (1996a)
Recovery rate (carriers)	$\gamma_2$	0.025 per year	Edmunds <i>et al.</i> , (1996a)
The proportion of those with acute infection that become a carrier	$p$	0.05	Edmunds <i>et al.</i> , (1996a)
Relative infectiousness of carriers	$\delta$	0.16	Edmunds <i>et al.</i> , (1996a)

### 6.2.3 Sensitivity Analysis

To test the effect of the model assumptions on the results obtained from the model a number of different tests of sensitivity were undertaken, these are listed below:

1. Alternative values for the FOI in new initiates and experienced IDUs were applied. These estimates taken from Chapter 5 are the values of the upper and lower 95% CIs of the baseline values, and an estimate of the FOI that is equal for both new initiates and experienced IDUs (Upper, Lower, and Equal). These are shown in Table 6.3:

Table 6.3 - FOI estimates (/person/yr) used during sensitivity analysis

<i>FOI</i>	$\lambda_1$	$\lambda_2$
Upper	0.1327	0.0590
Lower	0.0840	0.0198
Equal	0.0476	0.0476

2. To test the assumption of proportional mixing, the effects of alternative values of the transmission coefficients on model results were investigated. The first set of values assume that new initiates and experienced IDUs mix at the same rate as experienced IDUs mix amongst themselves (Mixing One), and the second set of values assumes that there is no mixing between new initiates and experienced IDUs (Mixing Two). The mixing matrices for each of these mixing assumptions (using the baseline FOI) is summarised in Table 6.4:

Table 6.4 - Values of the transmission coefficients (/yr) used during sensitivity analysis for: a) Mixing One and b) Mixing Two.

a) Mixing one	i=1	i=2	b) Mixing Two	i=1	i=2
i=1	$2.83 \times 10^{-4}$	$4.49 \times 10^{-5}$	i=1	$2.20 \times 10^{-4}$	
i=2	$4.49 \times 10^{-5}$	$4.49 \times 10^{-5}$	i=2		$3.02 \times 10^{-5}$

#### 6.2.4 Vaccination Scenarios

Three vaccination scenarios describing the potential future of the HBV vaccination programme in prisons in England and Wales are taken forward from Chapter 4 and applied here. Further scenarios are also examined here with a summary of the vaccination scenarios implemented provided in Table 6.5. The vaccination rates for the vaccination scenarios are calculated from the results obtained from the model of the prison vaccination programme (Chapter 4). They are for those IDUs that receive 2 or more doses of HBV vaccine and incorporate the possibility that an IDU may be vaccinated either in the community or in prison. It is assumed that an IDU is protected from HBV if they have received 2+ doses of vaccine. The rates for a selection of the scenarios stratified by year and injecting career length are shown in Table 6.6 and Table 6.7. Experienced IDUs are more likely to have been incarcerated in the past than new initiates, and as recidivists are more likely to go to prison than first time offenders, this explains the higher vaccination rates for experienced IDUs compared to new initiates which can be seen for all scenarios (Table 6.6 and Table 6.7). As the focus of this study is the impact of prison vaccination, the vaccination rate for IDUs in the community is taken at a constant value for all vaccination scenarios estimated to be 0.106/IDU/year as calculated in Chapter 4. For all vaccination scenarios where vaccination is administered on prison reception, at each vaccination event 38% receive 1 dose of vaccine, 28% receive 2 doses of vaccine, and 34% receive 3 doses of vaccine (Chapter 4).

Table 6.5 - Summary of vaccination scenarios

Vaccination Scenario	Description
England and Wales (Scenarios A, B, and C)	Taking the vaccination scenarios first described in Chapter 4, vaccination coverage is administered to prisoners on reception into prison. Coverage is 5% in 2002, 10% in 2003 and then a linear increase up to 33% for scenario A, 50% for scenario B (baseline scenario), and 66% for scenario C in 2006. Coverage is constant thereafter (Table 6.6).
Age Specific	Vaccination coverage is administered from 2002 on reception into prison targeting specific age groups. The age groups independently targeted are 15-17 years, 18-29 years or 30+ years with coverage that is constant over time of 30%, 70% or 100%.
Equilibrium	Vaccination coverage is administered on reception into prison from 2002 onwards at a constant rate until equilibrium has been reached. A number of alternative levels of vaccination coverage are examined to see which would result in the HBV prevalence (IDUs ever infected) reaching zero (Table 6.7).
Campaign	90% of prisoners receive 3 doses of vaccine in 2003, and then from this point on vaccination on reception into prison is introduced at 80% coverage. This represents a possible scenario where a strong commitment to vaccinate all prison inmates is introduced as was the case recently in Scotland (Hutchinson <i>et al.</i> , 2004). An alternative to this scenario sees 90% of prisoners receive 3 doses of vaccine in 2003, 2006, and 2009 with no further vaccination administered in prison.

**Table 6.6 - Vaccination rates / IDU / year for scenarios A, B, and C for England and Wales applied to new initiates and experienced IDUs.**

New Initiates				Experienced IDUs		
Scenario:						
Year	A	B	C	A	B	C
2002	0.01	0.01	0.01	0.13	0.13	0.13
2003	0.02	0.02	0.02	0.13	0.13	0.13
2004	0.04	0.04	0.04	0.13	0.13	0.13
2005	0.06	0.07	0.09	0.14	0.14	0.14
2006	0.08	0.11	0.14	0.15	0.15	0.15
2007	0.11	0.15	0.20	0.16	0.17	0.18
2008	0.11	0.16	0.21	0.17	0.19	0.22
2009	0.11	0.16	0.21	0.19	0.21	0.24
2010	0.12	0.17	0.22	0.19	0.23	0.26
2011	0.12	0.17	0.22	0.20	0.24	0.28
2012	0.12	0.17	0.22	0.21	0.24	0.28
2013	0.12	0.18	0.23	0.21	0.25	0.29
2014	0.13	0.18	0.23	0.21	0.25	0.29
2015	0.13	0.18	0.23	0.21	0.25	0.29

*Where each scenario assumes a vaccination coverage of 5% on prison reception in 2002, 10% in 2003 and then a linear increase of up to constant 33% in 2006 for Scenario A, 50% for Scenario B, and 66% for Scenario C (Chapter 4).*



**Table 6.7 - Vaccination rates / IDU / year for the equilibrium scenarios applied to new initiates and experienced IDUs.**

Vaccination coverage on prison reception	New Initiates	Experienced IDUs
5%	0.03	0.14
10%	0.05	0.15
15%	0.07	0.17
20%	0.09	0.18
25%	0.11	0.19

### **6.3 Results**

The results for each of the vaccination scenarios described in the methods are shown below. In all cases HBV prevalence is defined as the proportion of IDUs in the overall population that have ever been infected by HBV i.e. have antibodies to HBV (anti-HBc), while the acute infections here may be symptomatic or asymptomatic.

#### **6.3.1 England and Wales Scenarios**

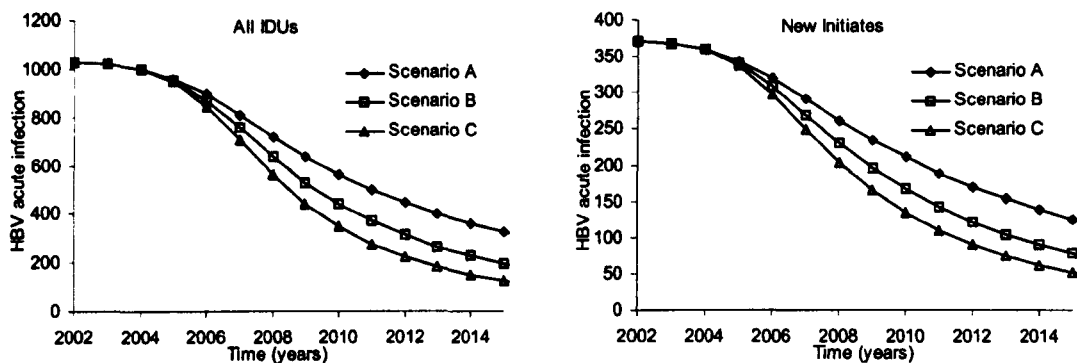
Prior to the introduction of the prison vaccination programme it is estimated that despite the presence of community vaccination there were over 350 new initiates and over 1000 experienced IDUs acutely infected from HBV in England and Wales in 2002. The overall HBV prevalence in the IDU population in 2002 was estimated to be approximately 15% with the HBV prevalence in new initiates and experienced IDUs being 9% and 17% respectively.

If there had been no community vaccination prior to 2002, then it is estimated that the prevalence of HBV in 2002 in the IDU population would be over 18% (approximately 9% and 20% in new initiates and experienced IDUs respectively). No community vaccination would lead to the annual number of acute infections in new initiates and experienced IDUs being estimated at 400 and 900 respectively. The

reduction in the number of acute infections in experienced IDUs in the no community vaccination scenario compared to the community vaccination scenario being due to many more IDUs being infected as new initiates.

The impact of prison vaccination on the incidence of HBV in new initiates and experienced IDUs within the overall IDU population of England and Wales is shown in Figure 6.1. The results show that as the vaccination rate increases over time the incidence of HBV in both new initiates and experienced IDUs decreases over time. A high proportion of the total number of acute infections of HBV in new initiates can be seen with over 30% occurring in the new initiates across all years.

Figure 6.1 - The estimated annual number of acute infections of HBV in the IDU population and new initiates.

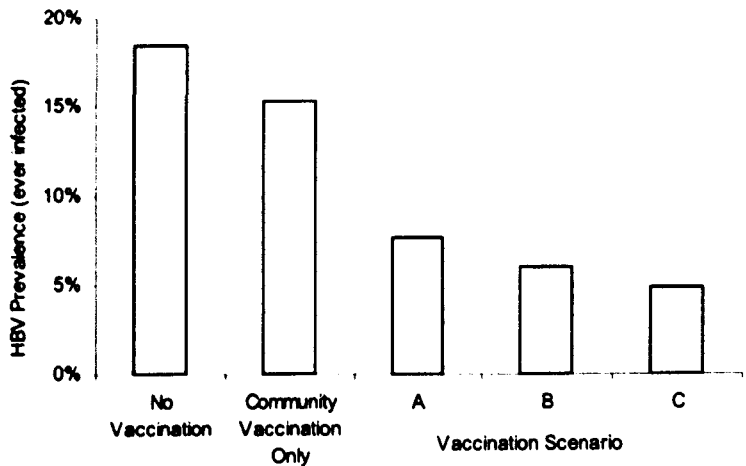


The implementation of the baseline vaccination scenario (scenario B) results in the total number of acute cases of HBV being reduced by approximately 35% by 2008 and then by approximately 75% in 2014. If vaccination coverage can reach 66% of all prison receptions by 2006 (scenario C) then the total acute cases within the IDU population can be reduced by approximately 45% in 2008 and 85% by 2014. However even if the vaccination coverage on prison reception only reaches 33% of all prison receptions by 2006 (scenario A) then the total acute cases within the IDU population will still be reduced by approximately 30% in 2008 and 60% by 2014.

The impact of the England and Wales scenarios on HBV prevalence in England and Wales in 2015 is shown in Figure 6.2. It can be seen that assuming that the

characteristics of the IDU population do not change over this period and there is no vaccination either in prison or the community, the HBV prevalence in 2015 will be approximately 18%. If vaccination is implemented on reception into prison and coupled with community vaccination (scenarios A, B, and C), it is estimated that HBV prevalence in the IDU population can be reduced to fewer than 10% by 2015.

Figure 6.2 - The estimated HBV prevalence in IDUs in 2015 with variations in the vaccination scenario implemented.



### 6.3.2 Age Specific Scenarios

The impact of applying alternative age specific vaccination scenarios on the HBV prevalence in the IDU population in 2015 is shown in Table 6.8. It can be seen that a targeted vaccination strategy targeting 18-29 years which represents 49% of the prison population at 30% coverage has a substantial effect on HBV prevalence reducing it by almost 50%. In the case of the 15-17 year olds, it is unsurprising to find that targeting this age group was the least effective vaccination strategy given that this age group represents only 4% of the prison population. However despite approximately 47% of the prison population being represented by over 30 year olds (Home Office, 2003), targeting this age group for prison vaccination was still found to be largely ineffective.

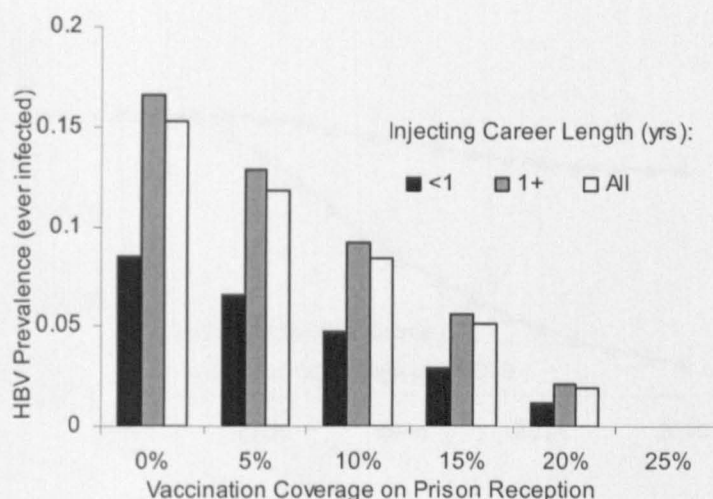
**Table 6.8 - The impact of alternative age specific vaccination scenarios on the HBV prevalence in the IDU population in 2015**

<b>Coverage</b>	<b>Age Group Vaccinated</b>			
	<b>15-17</b>	<b>18-29</b>	<b>30+</b>	<b>All</b>
<b>0.0</b>	15.3%	15.3%	15.3%	15.3%
<b>0.3</b>	13.9%	8.8%	13.7%	7.3%
<b>0.7</b>	12.4%	4.9%	12.9%	3.6%
<b>1.0</b>	11.5%	3.5%	11.5%	2.6%

### **6.3.3 Equilibrium Scenario Results**

It can be seen from Figure 6.3 that the HBV prevalence within the IDU population may reach zero when the vaccination coverage on prison reception is between 0.2 and 0.25 / prisoner / year. While this result is subject to a number of caveats and may not occur for many years (000s) it does show the potential long term impact of the HBV vaccination programme on prison reception on HBV transmission within the IDU population.

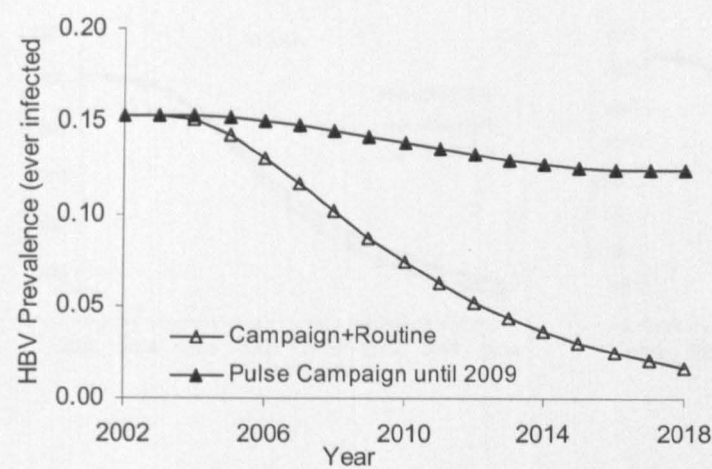
Figure 6.3 - The relationship between the vaccination coverage on prison reception and the post vaccination equilibrium



#### 6.3.4 Campaign Scenarios

The impact of two alternative campaign vaccination scenarios described in the methods is shown in Figure 6.4. It can be seen that if a campaign is administered in 2003 and this is followed up by a high level of vaccination coverage on prison reception, this can have a significant effect on the HBV prevalence within the IDU population dropping to less than 2% within 15 years. The impact of administering a vaccination campaign every three years from 2003 until 2009 is shown in Figure 6.4. It can be seen that while this strategy does have a positive effect on HBV prevalence, if this is not sustained, then 9 years after the final pulse vaccination the HBV prevalence once again begins to rise.

Figure 6.4 - The impact of alternative campaign vaccination scenarios on the prevalence of HBV within the IDU population over time.



### 6.3.5 Sensitivity Analysis

The effect on the baseline vaccination scenario of varying the estimated FOI in new initiates and experienced IDUs is shown in Figure 6.5. It can be seen that alternative values of the FOI have the potential to have a substantial effect on the HBV incidence estimates obtained from the model.

Figure 6.5 - The estimated annual number of acute infections of HBV in the IDU population with variations in the estimated FOI.

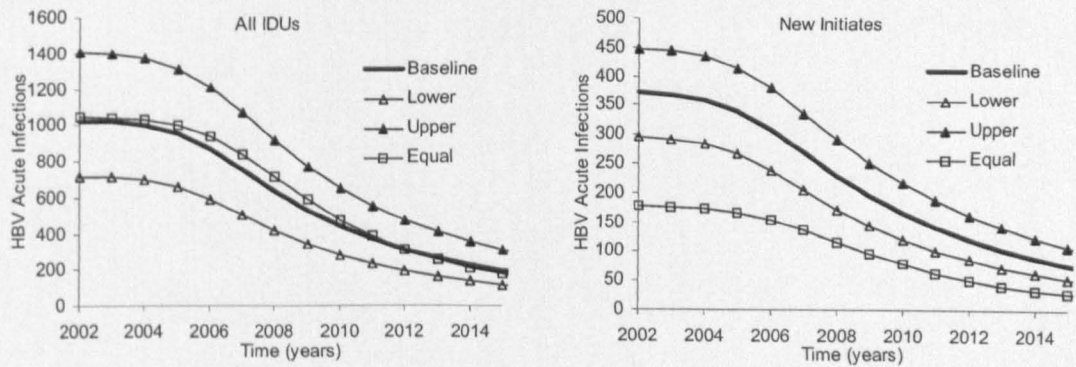
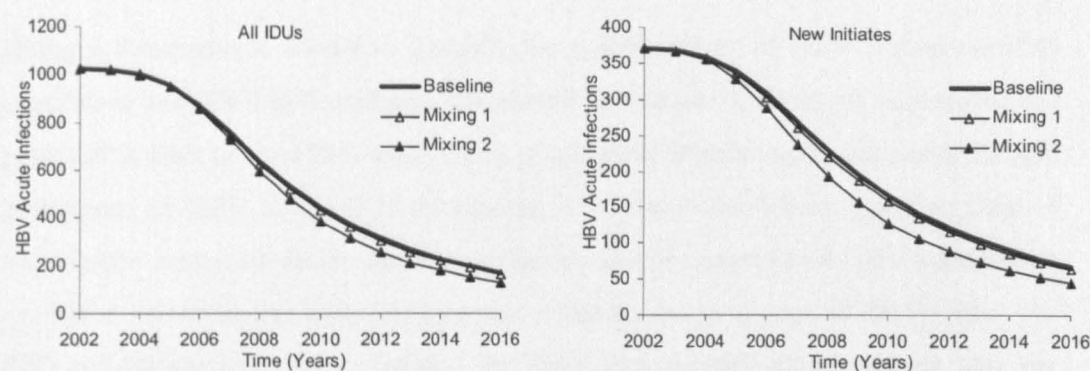


Figure 6.6 - The estimated annual number of acute cases in the IDU population with variations in estimations of the transmission coefficients.



The impact of varying the proportional mixing assumption is shown in Figure 6.6. It can be seen that either assuming that the rates of mixing are dominated by experienced IDUs (Mixing 1) or assuming that there is no mixing between new initiates and experienced IDUs (Mixing 2) has very little impact on the estimated number of acute cases of HBV in the IDU population.

## **6.4 Discussion**

Using a deterministic model to describe the epidemiology of HBV within the IDU population and HBV FOI estimates calculated in Chapter 5, the work here shows the potential impact of the HBV vaccination programme in prisons on the incidence and prevalence of HBV in the IDU population in England and Wales. Over a range of vaccination scenarios the model shows that increased coverage of HBV vaccination on prison reception can have a substantial effect on the incidence of HBV within the IDU population over time. Indeed, the base case model (that assumes that the vaccination coverage on prison reception is 5% in 2002, 10% in 2003 and then increases linearly up to 50% of prison receptions being vaccinated by 2006) predicts that the incidence of HBV in IDUs might be reduced by approximately 75% in 12 years from over 1,000 acute cases down to less than 300.

It has been assumed that the IDU population can be divided into two groups, those new initiates with an injecting career length of less than 1 year, and experienced IDUs with an injecting career length of greater than 1 year. This finding can be justified when considering the FOI estimates obtained in Chapter 5 which are substantially higher in new initiates compared to more experienced IDUs. While it is acknowledged that this is almost certainly an over simplification of the process by which IDUs interact, its simplicity makes model parameterisation easier based on data currently available.

Chapter 5 showed that no statistically significant variation in the FOI over time in IDUs was detected from 1999-2003. It has therefore been assumed that there is no variation in the FOI through time prior to the introduction of prison vaccination. Although as has been shown here the impact of using a dynamic model in which the FOI is not fixed inevitably results in a decrease in the FOI over time when vaccination is introduced.

Over a range of vaccination scenarios the results from this model have shown that an increase in the vaccination coverage on prison reception results in a reduction in the



number of acute cases of HBV in both new initiates to injecting and in experienced IDUs over time. Allowing for community vaccination the total number of acute HBV infections in 2002 in the IDU population in England and Wales was estimated from the model to be approximately 1,000 this includes all acute cases of HBV both asymptomatic and symptomatic. To verify this result it can be compared to the number of acute cases of HBV in England and Wales with a risk factor associated with injecting drug use as reported to the HPA in 2002 (Health Protection Agency, 2006), this was found to be 193. However after adjusting for under-reporting (Ramsay *et al.*, 1998) and asymptomatic infection (Hahne *et al.*, 2004), the annual number of acute infections is estimated at 1,100 cases, suggesting that the model is providing a reasonable estimation of the number of acute HBV infections in the IDU population in England and Wales.

The impact on the HBV prevalence within the IDU population over a range of hypothetical vaccination scenarios was also investigated. It was found that targeting the 18-29 age group had the greatest impact on HBV prevalence, compared to the 15-17 age group and 30+ age groups. Although targeting age groups of different sizes will inevitably favour the larger age groups it is likely that this result is due to the majority of current IDUs being aged from 18-29. However the model of the HBV vaccination programme in prisons assumes that the likelihood of starting injecting is the same irrespective of imprisonment status, whereas it is likely that persons that have previously been imprisoned are more likely to start injecting than those that have not. This suggests that the impact on HBV prevalence of vaccinating young prisoners may be underrepresented here.

The equilibrium scenarios were examined to see what levels of constant vaccination coverage on prison reception would result in the HBV prevalence reducing to zero. It was found that under base case assumptions a vaccination rate of between 20-25% would ultimately result in the HBV prevalence in the IDU population reducing to zero. While this result is interesting it is subject to a number of caveats. It is assumed both that the characteristics of the IDU population both inside and outside prison and the characteristics of the prison population are reasonably approximated here and remain constant over the same time period, which is unlikely particularly given that

equilibrium is not reached for thousands of years. While these are important caveats and should not be overlooked it does show that prison vaccination on reception has the potential to impact upon HBV prevalence within the IDU population in a substantial way.

The assumption that there is proportional mixing between new initiates and experienced IDUs was tested during the sensitivity analysis. It was assumed that the rate that the two groups interact was dominated by experienced IDUs, and alternatively it was assumed that there was no mixing between the groups. In each case it was found that the model results are not sensitive to these changes.

As has already been discussed the FOI estimates were taken from a previous analysis of IDUs in contact with services (Chapter 5), to test their impact on model results alternative plausible FOI estimates were substituted (Chapter 5). It was found that the FOI estimates have a major impact on the results obtained from the model particularly when the FOI is estimated to be the same in both groups suggesting that future work should be aimed at verifying these parameter values. It was assumed that the FOI estimates applied here were the same both inside and outside prison, while this is a bold assumption, obtaining data from which prison and community specific FOI estimates can be estimated will always prove problematic. As better FOI estimates become available that can distinguish the risk of infection both inside and outside prison, these can be incorporated into the model.

To verify whether the results obtained from this model are a reasonable estimation of the impact of the HBV vaccination programme in prisons on the transmission of HBV in the IDU population, reports of acute cases of HBV that are reported to the HPA in future years can be compared to the results presented here. Allowing for asymptomatic infection and underreporting, it will then be possible to verify whether the estimated impact of the HBV vaccination programme in prisons on HBV transmission in the IDU population in England and Wales is correct.

An important caveat within this work is that HBV transmission by non-IDUs has not been explored within this model. While it is likely that HBV will never be eradicated

in the IDU population due to transmission from non-IDUs to IDUs, prison vaccination will inevitably capture many non-IDUs that have increased risk factors from HBV infection e.g. sex workers and this will have a positive impact on HBV transmission within the overall population of England and Wales.

This chapter concludes the research investigating the impact of the HBV vaccination programme in prisons in England and Wales on the IDU population. However as has already been discussed IDUs are also at increased risk of infection from HCV and prison may also be a good location in which to target IDUs against this BBV. This will be the subject of Chapter 7.

**The research in this chapter has been published in full in the following peer reviewed article:**

**Sutton, A. J., Gay, N. J., & Edmunds, W. J. (2006).** Modelling the impact of prison vaccination on hepatitis B transmission within the injecting drug user population of England and Wales. *Vaccine* **24**, 2377-2386.

## **CHAPTER 7 - ESTIMATING THE COST-EFFECTIVENESS OF DETECTING CASES OF CHRONIC HEPATITIS C INFECTION ON RECEPTION INTO PRISONS**

### **7.1 Aims and introduction**

- To estimate the cost per HCV case detected under a range of screening scenarios implemented on reception into prisons in England and Wales.
- To estimate the proportion of the IDU population that is HCV-RNA positive that might be screened on reception into prisons in England and Wales.
- Using sensitivity analysis, identify the parameters that have the greatest impact on the estimated cost per HCV case detected.

Previous chapters have shown that prison may be a good location in which to vaccinate IDUs against HBV and that this intervention may have a significant impact on the transmission of HBV within the IDU population of England and Wales. It has also been shown amongst the reported laboratory diagnoses of HCV infection in England in 2004, 95% of those with exposure data were attributable to injecting drug use (Health Protection Agency *et al.*, 2005). The advantages of identifying individuals with undiagnosed HCV infection have already been discussed in section 1.3.1.2. By applying the model of the flow of IDUs through prisons in England and Wales (Chapter 3) in a different setting, in this chapter the effectiveness of HCV case-finding on prison reception is examined.

An analyses in which costs are related to a single, common effect which may differ in magnitude between the alternative programmes, is usually referred to as cost-effectiveness analyses (Drummond *et al.*, 1997). In this case the cost effectiveness of a range of alternative HCV case-finding scenarios implemented on reception into prisons in England and Wales to identify persons infected by chronic HCV (HCV-RNA positive) is investigated. Each scenario is compared by considering the cumulative cost of identifying a new case of HCV (HCV-RNA positive) and how

this cost changes over time as previously tested individuals return to prison. Incremental cost-effectiveness analysis is also undertaken.

## 7.2 Methods

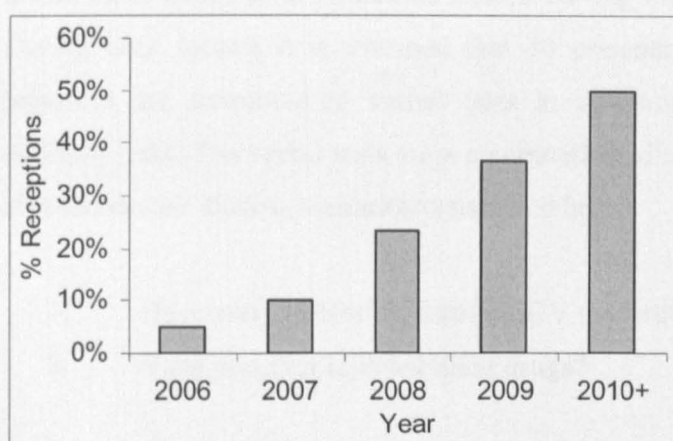
### 7.2.1 Model Structure

The model here is adapted from the model of the flow of IDUs and non-IDUs through prisons described in Chapter 3. The current IDU population described here has been subdivided into new initiates to injecting and experienced IDUs. New initiates to injecting are defined as those IDUs with an injecting career length of less than a year, and experienced IDUs are those individuals with an injecting career length of greater than one year. The FOI estimates for both new initiates and experienced IDUs are taken from Chapter 5. It is assumed that the FOI rates are constant over time and independent of prison status. While it is acknowledged that the risk of BBV infection amongst IDUs inside prison may be significantly higher than in the community (Macalino *et al.*, 2004), reliable FOI estimates that distinguish between prison status have not been obtained. Due to the small proportion of HCV infections that have an identified risk factor other than injecting drug use in England and Wales (Health Protection Agency Centre for Infections, 2005), it is anticipated that the FOI in non-IDUs will be extremely low, and so for this reason it is assumed that only IDUs can become infected by HCV with the incidence of new infections in the general population (non-IDUs) assumed to be zero. For those persons that are infected by HCV it is assumed at the time of infection that 80% (Health Protection Agency, 2006) become HCV RNA positive, although this assumption will be tested during sensitivity analysis.

### 7.2.2 HCV Case-finding Coverage

Currently there is no significant ongoing HCV case-finding on reception into prisons across England and Wales. It is assumed therefore that HCV case-finding coverage on prison reception is expanded over time to reflect the rolling out of an HCV case-finding programme across prisons in England and Wales. Figure 7.1 shows the percentage of prison receptions in England and Wales where case-finding is undertaken over time assumed in this analysis.

Figure 7.1 - Assumed proportion of prison receptions covered by HCV case-finding



### 7.2.3 Case-finding Pathway on Prison Reception

The case-finding pathway through prison reception proposed here is taken directly from a previous study using publicly available information describing the implementation of screening and treatment of HCV in the Isle of Wight prison cluster (Skipper *et al.*, 2003) although treatment is excluded from the pathway considered here. The study of the Isle of Wight Prison Cluster considers prisoners as they first attend a one hour health awareness lecture during which they are alerted to the risk factors for BBVs and are then invited to the Healthwatch clinic which was set up in 1997 to provide counselling on BBVs for all new receptions to the Isle of Wight prisons. Testing and counselling undertaken in the Healthwatch clinic on reception as described in the Isle of Wight Study are applied here and described below (Figure 7.3 and Figure 7.4). In addition verbal tests are introduced along the screening pathway to investigate whether alternative HCV case-finding strategies may be more cost effective than offering testing to all individuals. Prisoners are given verbal tests regarding their previous injecting behaviour and results of previous HCV testing, with the answers to these questions used to judge whether the prisoners are eligible to receive serological HCV tests to establish their HCV status.

The case-finding pathway is described in Figure 7.3 and Figure 7.4 and applies to all prisoners that are amongst the proportion on reception that are covered by the HCV

case-finding programme (Figure 7.1). Initially all prisoners on reception into prison attend a one hour health awareness lecture alerting them to the risk factors of BBVs. During each lecture it is assumed that 10 prisoners are present. Following this, prisoners are submitted to verbal tests to determine their eligibility to receive antibody tests. The verbal tests are a combination of the following, and represent the alternative case-finding scenarios considered here:

1. Have you received a positive HCV test previously?
2. Have you ever injected illicit drugs?

The first question is asked to establish whether the prisoner has been previously diagnosed with HCV. This question specifically asks about a previous positive test rather than simply a previous test, as a previous negative test is of limited interest as the prisoner may have been exposed to HCV in the mean time. The 2<sup>nd</sup> question is used to establish whether the person has ever injected illicit drugs. Where verbal questioning is administered (scenarios one to three, see below), the time taken to question the prisoners is assumed to be independent of the number of questions asked and is assumed to take 5 minutes, although this will be examined during sensitivity analysis. Previous studies (Schlichting *et al.*, 2003; Best *et al.*, 1999; Darke, 1998) have considered the sensitivity and specificity of IDUs responses to questions related to HCV positivity and the self-reporting of their illicit behaviours. The values taken at baseline and applied during sensitivity analysis are described in Table 7.2.

Following the verbal tests those prisoners that have been identified as being eligible to receive serological testing are assumed to be offered pre-test counselling. For those prisoners that are willing to accept serological testing an enzyme linked immunosorbant assay (ELISA) antibody test is assumed to be administered. Prisoners identified as having a positive antibody test are assumed to be informed that they have evidence of contact with HCV and are then offered a polymerase chain amplification (PCR) test for the presence of HCV viral RNA as a marker of ongoing infection. Those who are positive for HCV by antibody testing but negative on a single PCR test are assumed to be offered two further PCR tests as was adopted



in the Isle of Wight Study (Skipper *et al.*, 2003), the costs of which are incorporated in the analysis.

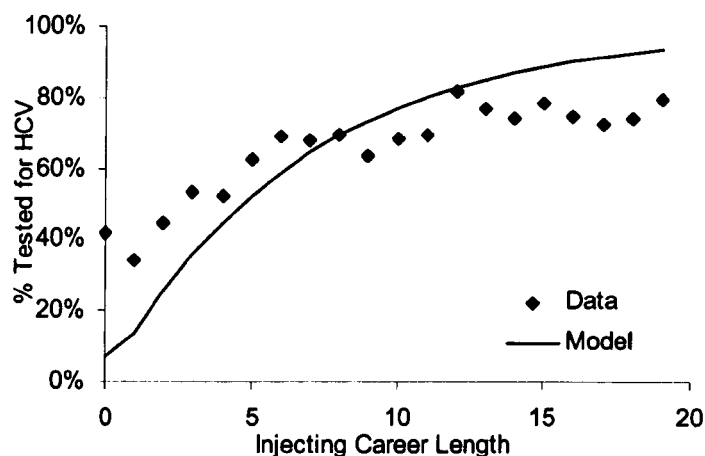
Post-test counselling is administered to all prisoners on receipt of the results from the ELISA and PCR tests. Those with positive tests are assumed to be counselled on harm reduction and harm minimisation. Assumed time and staff allocations for each task on the case-finding pathway are shown in Table 7.2, where no reference was available to inform these values, reasonable assumptions were made with the impact of these being examined during sensitivity analysis.

#### 7.2.4 Community HCV Testing and Diagnosis

As a result of drug treatment and prevention services in the community, it is possible for some HCV positive IDUs to become aware of their positive status as a result of testing in the community. Further to this, HCV positive individuals that develop symptoms associated with their infection may also have their HCV infection diagnosed in the community.

Data was considered from the UAPMP survey 2003-2004 of IDUs (who injected in the previous four weeks prior to the survey) reporting whether they had ever received a test for HCV by career length. Assuming that this data is representative of the IDU population in the community and that no HCV testing had been undertaken in prison, a model was fitted to the data using maximum likelihood fitting to binomial data (section 3.3.3). Amongst IDUs that are infected but undiagnosed the rate that IDUs in the community are tested and diagnosed for HCV was estimated to be 0.15 /IDU/ year, and while it is acknowledged that this model does not provide a good fit to the data (Figure 7.2) the impact of this parameter on model results will be investigated during sensitivity analysis.

Figure 7.2 - Model fit to UAPMP survey data 2003-2004 describing the % of current IDUs reporting receiving a previous HCV test



#### 7.2.5 Case-finding Scenarios

Varying the verbal questions asked on prison reception allows us to compare five alternative case-finding scenarios used to identify individuals that are eligible to receive an offer of serological testing for HCV (the ELISA and PCR tests offered being the same for scenarios one-four, see above). A negative answer to the question of previous injecting and a positive answer to the question of a past positive HCV test would indicate that the person is ineligible for HCV serological testing. The verbal screening that distinguishes each scenario is described in Table 7.1:

Table 7.1 - Summary of case-finding scenarios

Scenario	Description
One	Verbally screen for ever having received a past positive HCV test, and for ever having injected illicit drugs.
Two	Verbally screen for a past positive HCV test only.
Three	Verbally screening for ever injecting illicit drugs only
Four	No verbal screening
Five	No verbal screening and no testing (do nothing scenario)

Comparisons are made between each case-finding scenario by considering the cumulative cost per chronic HCV case (RNA positive) detected and how this varies over time. The complete parameter set describing the case-finding scenarios at baseline are shown in Table 7.2. The implication of these parameter selections on the model results are examined during sensitivity analysis with the values taken during sensitivity analysis also shown in Table 7.2. All costs are presented in year 2004 with discounting rates for both costs and benefits taken at 3.5% as recommended by the HM Treasury (HM Treasury, 2003) although the impact of these are varied during sensitivity analysis (Table 7.2). The analysis here is considered from the perspective of the health care provider.

Figure 7.3 - Schematic diagram of the case-finding scenarios used in this analysis

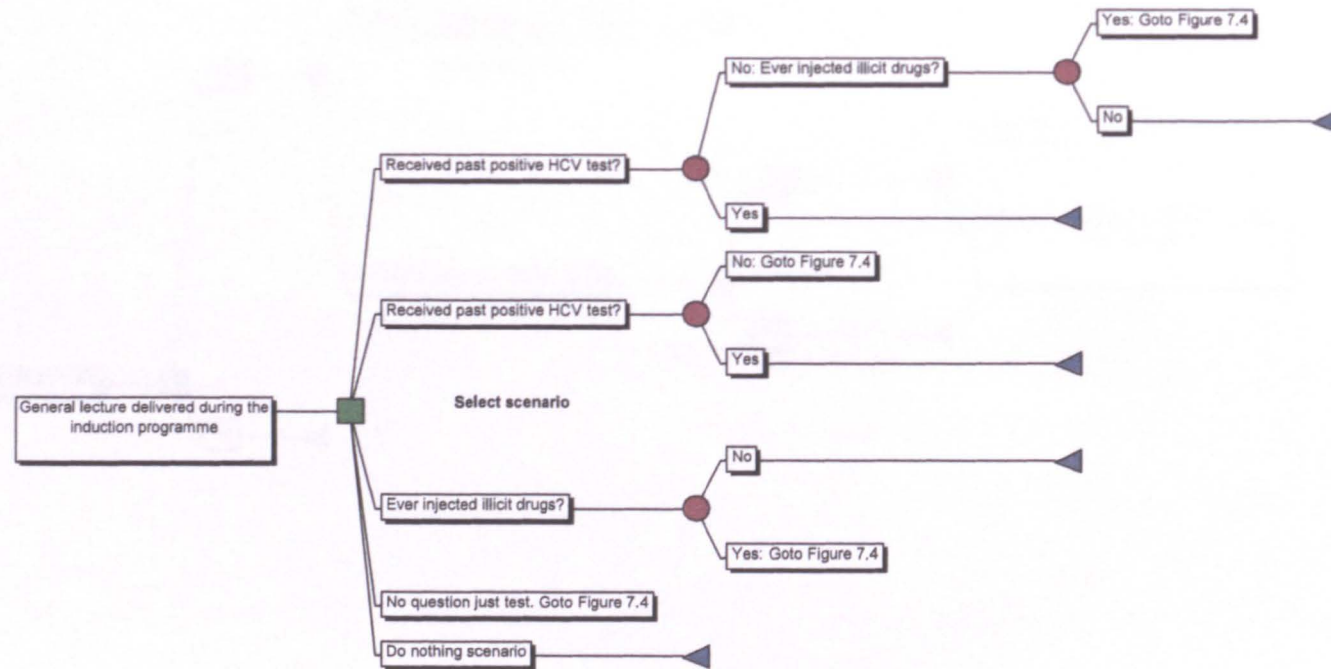


Figure 7.4 - Pathway describing the administering of HCV serological tests

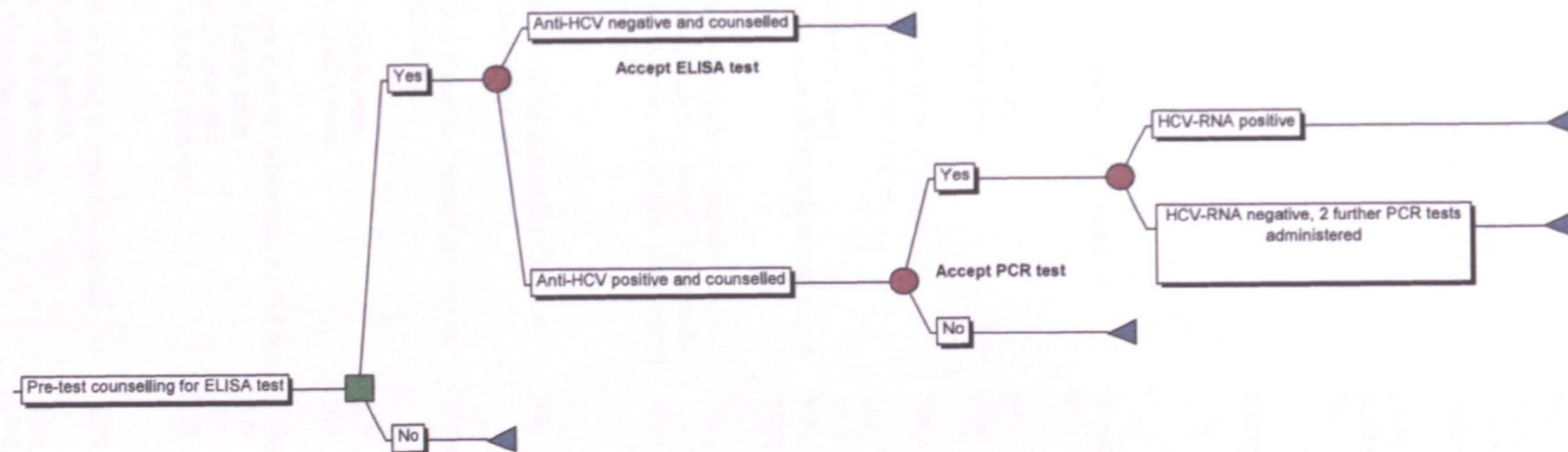


Table 7.2 - Model parameters and values used during sensitivity analysis

<i>Parameter</i>	<i>Baseline value</i>	<i>Sensitivity</i>	<i>Source (where available)</i>
$\lambda_0$ = FOI for new initiates	0.1608	0.1314-0.1942	Chapter 5
$\lambda_1$ = FOI for experienced IDUs	0.0526	0.0310-0.0863	Chapter 5
Cost of Doctor	£3.49 / min (£209.40 /hr)		GP: /home visit / min With Qualification costs With direct care staff costs(Curtis & Netten, 2004)
Cost of Nurse	£54 / hour		District Nurse (midpoint grade G) /hr with patient + extra costs (Curtis & Netten, 2004)
<i>Time Taken for BBV lecture / prisoner</i>	10 patients / hr	1 patient /hr – 20 patients / hr	(Skipper <i>et al.</i> , 2003)
% Nurse time	50%	0-100%	
% Doctor time	50%	0-100%	
<i>Time taken to verbal test on reception into prison</i>	5min	1-15min	(Stein <i>et al.</i> , 2002)
% Nurse time	50%	0-100%	(Stein <i>et al.</i> , 2002)
% Doctor time	50%	0-100%	(Stein <i>et al.</i> , 2002)
% who are HCV positive and say so	55% (midpoint)	23%-83%	23% (Schlichting <i>et al.</i> , 2003), 83% (Best <i>et al.</i> , 1999),
% never received a positive HCV test but say they are HCV positive	1%	0%-10%	
% IDUs that report IDU use (current or ever)	75%	30-90%	Darke, (1998) reports that IDUs give reasonably reliable answers to questions about drug use.
% non-IDUs that report IDU use (current or ever)	0%	0-20%	
<i>Time Taken to Counsel prior to an ELISA test</i>	25min	10-60min	25min (Leal <i>et al.</i> , 1999) 10-60min (Stein <i>et al.</i> , 2002)
% Nurse time	50%	0-100%	(Stein <i>et al.</i> , 2002)
% Doctor time	50%	0-100%	(Stein <i>et al.</i> , 2002)
<i>Time taken to Administer ELISA test</i>	5min	1-10min	
% Nurse time	50%	0-100%	
% Doctor time	50%	0-100%	
Cost of ELISA test	£12	£5-20	Virus reference department, HPA, Colindale (2005)
% of those offered who accept ELISA testing	85%	10-100%	(Stein <i>et al.</i> , 2002)
ELISA Sensitivity	97%	90-100%	(Stein <i>et al.</i> , 2002)
ELISA Specificity	99%	90-100%	(Stein <i>et al.</i> , 2002)
<i>Time taken to administer PCR test</i>	5min	1-10min	
% Nurse Time	50%	0-100%	
% Doctor Time	50%	0-100%	

% of those offered who accept PCR testing	100%	50%	Assuming that those that accept an ELISA test will then accept a PCR (Stein <i>et al.</i> , 2002)
PCR Sensitivity	100%	99%-100%	(Stein <i>et al.</i> , 2002)
PCR specificity	100%	99-100%	(Stein <i>et al.</i> , 2002)
Cost of PCR test	£57	£50-80	Virus reference department, HPA, Colindale (2005)
<i>Time taken to counsel the result of negative ELISA or PCR test</i>	5min	5-15min	
% Nurse time	50%	0-100%	
% Doctor time	50%	0-100%	
<i>Time taken to counsel the result of a positive ELISA test</i>	25min	15-75min	25min (Stein <i>et al.</i> , 2002) 15-75min (Stein <i>et al.</i> , 2002)
% Nurse time	50%	0-100%	
% Doctor time	50%	0-100%	
<i>Time taken to counsel the result of a positive PCR test</i>	25min	15-75min	25min (Stein <i>et al.</i> , 2002) 15-75min (Stein <i>et al.</i> , 2002)
% Nurse time	50%	0-100%	
% Doctor time	50%	0-100%	
Proportion infected with HCV that become HCV-RNA positive	80%	54%-86%	(Seeff, 2002;Health Protection Agency, 2006)
Rate of HCV testing and diagnosis in the community	0.15	0.1-0.3	See text
Discount rate for costs	3.5%	0%-6%	(HM Treasury, 2003)
Discount rate for benefits	3.5%	0%-6%	(HM Treasury, 2003)

### 7.3 Results

It can be seen (Figure 7.5c) that scenario one: identifying those individuals that have not received a past positive HCV test, and have ever injected illicit drugs is the most cost effective scenario over time. This shows the importance of identifying those individuals with a history of injecting drug use, which is the biggest risk factor for HCV infection. Least cost effective is scenario two: only identifying those individuals that have not received a past positive HCV test. For all scenarios the cost per new HCV case detected rises over time indicating that they become less cost effective as time passes. This is due to IDUs returning to prison that are already aware of their HCV infection, leaving a smaller proportion of individuals on reception into prison that have undiagnosed infection.

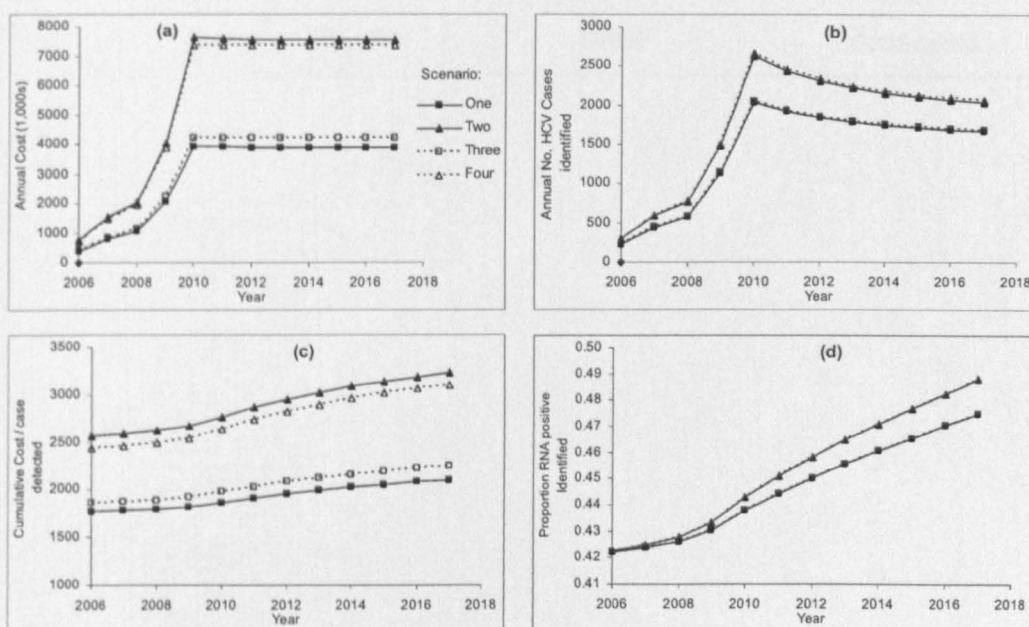
The undiscounted cost of implementing each case-finding scenario is shown in Figure 7.5a. For each case-finding scenario the cost increases up to a plateau in 2010 and then is broadly constant from then on. The initial increase and then plateau can be explained by the assumed expanding coverage of HCV case-finding on prison reception over time up to a constant coverage from 2010 onwards (Figure 7.1). It can be seen that scenarios two and four are far more costly than the remaining scenarios, however neither of these scenarios screen prisoners on prison reception for any previous injecting drug use, and as a consequence many more ELISA and PCR tests are administered for scenarios two and four than are necessary. A slight reduction in the cost was observed in scenarios one and two from 2010 onwards, this is due to persons having been diagnosed with HCV infection returning to prison and then being verbally screened for a past positive HCV test, hence reducing the costs further along each of the case-finding pathways.

From Figure 7.5d it can be seen that scenarios two and four identify the greatest proportion of individuals that are HCV-RNA positive over time, however these scenarios are not very cost effective due to the high costs required to administer them.



Results from the incremental analysis are reported in Table 7.3, where the alternative strategies have been ranked according to their cumulative discounted cost in 2017 and the incremental cost-effectiveness ratios have been calculated. This highlights that scenario two is the most cost-effective option and has the smallest budget impact (least cost).

Figure 7.5 - The results for the first four case-finding scenarios compared with the current do nothing (no HCV case-finding in prisons) strategy



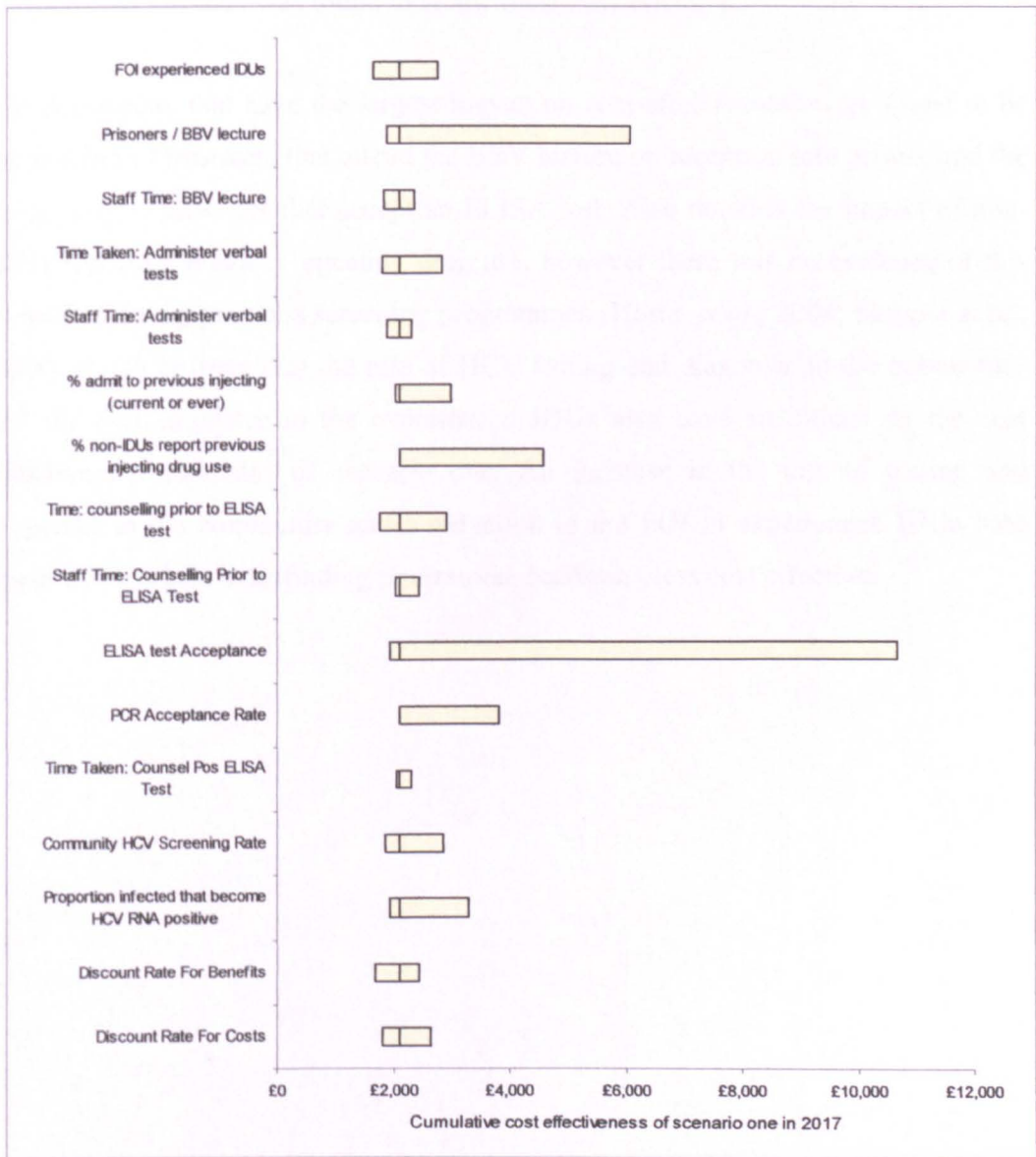
Taking parameter values at baseline values (Table 2). a) the undiscounted annual cost of implementing each case-finding scenario, b) the undiscounted annual number of new HCV cases identified when implementing each case-finding scenario, c) the cumulative average cost per new HCV case detected with discounting, d) the proportion of those HCV-RNA positive that are identified over time.

**Table 7.3 - Incremental cost effectiveness analysis of each case-finding scenario**

<i>Case-finding Scenario</i>	<i>Cumulative discounted cost in 2017 (1,000s)</i>	<i>Cumulative discounted no. of cases of HCV identified in 2017</i>	<i>Incremental Cost Effectiveness</i>
Five (Do Nothing)	£0	0	
One	£28,192	13413	£2,102
Three	£30,444	13548	£16,681
Four	£53,123	17098	£6,388
Two	£54,670	16927	dominated

### 7.3.1 Sensitivity Analysis

Figure 7.6 - The impact on the cumulative average cost effectiveness of scenario one in 2017 compared to the current no case-finding strategy when applying one-way sensitivity analysis (section 2.2.4).



*The bars represent the costs when the upper and lower parameter estimates are implemented while the line through each is the baseline value.*

Figure 7.6 shows the impact of one-way sensitivity analysis on the cumulative average cost per case detected in 2017 for case-finding scenario one compared with the current do nothing policy. In each case only those parameters that impact on the baseline value by greater than 10% are shown. It can be seen that in many cases the parameter values have little impact on the cost effectiveness of this scenario and in all cases this scenario was found to be the most cost-effective.

The parameters that have the largest impact on cost-effectiveness were found to be the number of prisoners that attend the BBV lecture on reception into prison, and the proportion of prisoners that accept an ELISA test. Also noted is the impact of non-IDUs reporting previous injecting drug use, however there was no evidence of this occurring during previous screening programmes (Horne *et al.*, 2004; Skipper *et al.*, 2003). It can be seen that the rate of HCV testing and diagnosis in the community and the FOI estimates in the experienced IDUs also have an impact on the cost effectiveness estimates of scenario one. An increase in the rate of testing and diagnosis in the community and a reduction in the FOI in experienced IDUs both result in the prison case-finding programme becoming less cost effective.

## **7.4 Discussion**

Using a Markov decision analysis model, a model of the flow of IDUs through prisons in England and Wales (Chapter 3), and estimates of the FOI for HCV in the IDU population (Chapter 5) the chapter here investigates the cost effectiveness of a number of alternative HCV case-finding strategies including verbal screening for ever injecting drug use and for previous HCV testing. Results indicate that verbally screening for ever injecting illicit drugs and for ever having received a past positive HCV test is the most cost effective approach to establishing prisoners eligible for serological testing, while sensitivity analysis found that the proportion of eligible prisoners that accept ELISA testing has a significant impact on the cost-effectiveness of the case-finding scenarios.

A typical approach to a cost-effectiveness analysis such as this would be to adopt a simple spreadsheet model in which a hypothetical cohort of individuals (usually modelled as being at the same age) would be modelled flowing into prison, however this approach would not allow the impact of previously screened individuals returning to prison to be investigated. This is of particular significance here as it has been found that the case-finding scenarios described here all become less cost-effective over time, this being due to previously screened individuals returning to prison that do not need re-screening and the time taken to identify these prisoners. Although a reduction in annual costs were noted over time in some of the case-finding scenarios due to prisoners that had already received a positive serological test being identified on prison reception. For each scenario when the proportion of prison receptions covered by HCV case-finding had been assumed to have reached a constant the costs and benefits over time display only relatively small variation.

It is possible for an individual to become HCV-RNA positive during a spell of imprisonment, this may occur for two reasons, either the individual was infected while in prison or the individual was infected outside prison but due to the natural history of HCV, HCV-RNA was not detectable on reception into prison. HCV-RNA can be detected within 1 to 2 weeks after exposure to the virus although HCV-RNA

positivity may appear much later at 30 to 40 days (World Health Organisation, 1999; Mortimer, 2000). As two further PCR tests are administered to those individuals that are anti-HCV positive but negative for HCV-RNA it is unlikely that individuals infected just prior to reception will remain undetected. If however it is felt that there is a significant risk of some prisoners becoming HCV-RNA positive while in prison, then to allow these individuals to be offered treatment or counselling it may be necessary to administer some HCV testing during an individuals prison sentence or perhaps on discharge from prison.

Results from sensitivity analysis showed the importance of encouraging eligible prisoners to accept the offer of an ELISA test, with a reduction in uptake having a large impact on cost-effectiveness. Intervention measures outside prison such as testing and diagnosis in the community or those that target IDUs aimed at reducing their at risk behaviour (and therefore the FOI) can have a negative impact on the cost-effectiveness of a prison based case-finding programme even, though a prison based programme may well be more cost-effective than a programme based in the community. This shows the importance of coordinating intervention measures inside and outside prison to ensure the maximum effectiveness of both.

The work here has focused on identifying those individuals that may be at risk from HCV infection and then offering them an HCV test as appropriate, however it is possible that an individual may encounter further problems if they admit to injecting drug use, this in many instances may take the form of the social stigma associated with injecting drug use. It is hoped that admitting to previous injecting drug use will be seen in a positive light as individuals can then be targeted for drug related intervention measures or HCV treatment if necessary. To allow for the possibility that individuals may not give reliable answers to questions regarding injecting drug use or HCV status a range of values describing the sensitivity and specificity to individuals answers related to previous HCV testing and injecting drug use were considered. It was found that of importance to model results were the answers that individuals gave to the issue of previous injecting behaviour. However it is hoped that the one hour health awareness lecture described at the start of the screening

pathway will provide a good opportunity in which to address individuals concerns regarding the revealing of potentially sensitive information.

A further account of screening for HCV in the prison population in England and Wales is described in a previous study considering the experience of screening in the Dartmoor prison (Horne *et al.*, 2004). In this study the authors describe data collected from a cohort of prisoners screened from 1 January 1998 to 30 June 2001 describing progress from test result to treatment. A key difference between the screening pathway described in Dartmoor compared to the Isle of Wight appears to be the additional two PCR tests administered at the Isle of Wight for those individuals that test anti-HCV positive but HCV-RNA negative after a first PCR test. This means that the costs of the scenarios reported here may be less cost-effective than if the requirement to implement these two additional PCR tests was removed.

The approach to staff costs in this work has considered only the role of a doctor and nurse in implementing the alternative case-finding scenarios, while the estimates of the length of time taken to undertake the individual tasks along the case-finding pathways are inevitably subject to much variation. Considering only doctors and nurses is an obvious over simplification, with other members of staff such as prison chaplains and guards playing a role in the implementation of a prison based case-finding programme. However in mitigation the results from the sensitivity analysis have shown that staff costs and length of time required to accomplish each task play only a small part in variation in the estimates of the cost-effectiveness of the case-finding scenarios.

While treatment has not been considered here, there are still advantages in identifying those individuals that are HCV-RNA positive. Any individual that is HCV-RNA positive obviously has the potential to transmit infection particularly if the person is an IDU and continues to inject illicit drugs. An awareness of the infected status of these individuals is useful to services as they can then be targeted for intervention measures aimed at reducing the behaviour that leads to further HCV transmission. This may take the form of encouraging injecting cessation or the supplying of clean needles to reduce the risk of transmission due to the sharing of

syringes. While identified HCV positive individuals themselves may choose to modify their own behaviour to prevent further transmission. A further advantage of HCV case-finding is that positive individuals can be monitored so that they can be treated when treatment criteria have been met, which in the case of IDUs will be when the individual has ended their injecting career (National Institute for Clinical Excellence Guidelines, 2004). Identification of HCV positive individuals on prison reception may also assist in identifying further positive individuals in the community through contact tracing exercises. However it is of some importance that those individuals that are identified with HCV infection are given post test support to come to terms with their infection. Previous studies have shown that knowledge of a past positive HCV test can have a negative impact on an individual's quality of life (Forman *et al.*, 2000; Rodger *et al.*, 1999; Chong *et al.*, 2003; Tompkins *et al.*, 2005) particularly when post-test support is not offered. This should be considered when weighing the pros and cons of adopting a case-finding programme such as this.

In summary, prison provides a good location in which to identify individuals previously infected by HCV. Verbally screening for individuals that have previously received a positive HCV test and for ever having injected drugs was found to be the most cost effective scenario. However it is expected that the cost-effectiveness of HCV case-finding will decrease over time as HCV infected individuals that have already been identified previously return to prison.

**The research in this chapter has been published in full in the following peer reviewed article:**

**Sutton, A.J.,** Edmunds, W.J., & Gill, O.N.(2006). Estimating the cost-effectiveness of detecting cases of chronic hepatitis C infection on reception into prison. *BMC Public Health* 6, 170.



## **CHAPTER 8 - DISCUSSION**

### **8.1 Introduction**

A variety of methods have been considered in this thesis that has helped to further knowledge about the characteristics of the IDU population and in particular its risk of infection from BBVs. The potential impact of a number of prison based intervention measures that target the IDU population in a prison setting has also been considered. These methods have included statistical and mathematical modelling techniques and also some economic evaluation. Statistical techniques have been used to obtain parameter estimates that have helped to understand the characteristics of the IDU population and its flow through prison. The impact of prison based intervention measures have been investigated through mathematical modelling. Moreover, an economic evaluation has been utilised to assess the cost-effectiveness of alternative HCV case-finding strategies on reception into prison.

### **8.2 Summary of main findings**

Younger IDUs are less likely to stop injecting than older IDUs suggesting that those individuals that embark on an injecting career at a younger age will inject for far longer than those that start injecting at an older age. The trend in the incidence of injecting in the male IDU population in England and Wales was estimated to peak in the early 1980s followed by a steep reduction down to a constant throughout the 1990s with a slight reduction in 2000-2001. This slight reduction in the number of males starting injecting coupled with an increase in the average injecting career length of an IDU in more recent years (1997-2001) may be indicative of a change in the nature of the IDU population with more 'problem' rather than casual users. This may have had an impact on the spread of BBVs within the IDU population of England and Wales in recent years and help to explain the rise of HBV and HCV prevalence since 2000 (sections 1.3.1.1 and 1.3.1.2).

To estimate the impact of a series of alternative intervention measures that target IDUs against BBVs in a prison setting a model of the flow of IDUs through prisons in England and Wales was designed and parameterised. This model provides estimates of the rate that IDUs and non-IDUs pass through prison, and then return to prison due to recidivist behaviour. Using this model it is then possible to estimate what proportion of the IDU population might be captured by prison based intervention measures particularly those aimed at BBVs, as is the focus of this thesis.

The parameterisation of the flow of IDUs through prisons in England and Wales provided further evidence that IDUs are at increased risk of imprisonment compared to non-IDUs. A comparison of the discharge rates for IDUs and non-IDUs show that IDUs spend less time in prison per spell of imprisonment compared to non-IDUs. For IDUs that have been imprisoned parameter values for the discharge rates and re-imprisonment rates were found to be constant across all age-groups, suggesting that much of the IDUs offending behaviour may be independent of age.

Under a range of vaccination scenarios applied to the model of the flow of IDUs and non-IDUs through prisons in England and Wales, the impact of the HBV vaccination programme in prisons on the vaccination status of current IDUs was estimated. Results showed that with increasing coverage on reception into prisons a greater proportion of the IDU population may be vaccinated against HBV. However, even with 100% vaccination coverage on reception a proportion of the IDU population will not be vaccinated as some IDUs will never go to prison. This shows the importance of ensuring that vaccination is also administered in the community, a finding that was verified during the sensitivity analysis that showed the importance of the community vaccination rate on estimates of the proportion of the IDU population captured by vaccination. Sensitivity analysis also showed the importance of the estimated discharge rate of IDUs from prisons and the estimated IDU population size on model results. A higher discharge rate will result in IDUs flowing through prisons faster and lead to a greater proportion of the IDU population being exposed to prison vaccination as individual IDUs return to prison. As it has been estimated from data what proportion of the prison population is defined as being a current IDU (Weild *et al.*, 2000) smaller estimates of the size of the IDU population

will result in a greater proportion of IDUs being vaccinated in prisons, as shown in the sensitivity analysis.

In order to inform the models that appear later in the thesis that describe the transmission of HBV in the IDU population and the cost-effectiveness of HCV case-finding in the IDU population, estimates of the FOI for HBV and HCV must be made. Using data from the UAPMP surveys of current IDUs in England and Wales the FOI for HBV and HCV and how this has varied over time and with injecting career length was estimated. The issue of individual heterogeneity within the IDU population was also addressed to determine whether certain individuals are at greater risk from infection than others independently of injecting career length or time.

Model estimates found that new initiates to injecting are at increased risk from BBVs compared to more experienced injectors, and that there is evidence of individual heterogeneity of risk behaviour where independently of the injecting career length effects, some IDUs are at increased risk of infection compared to others. A key question from this work is why the prevalence of BBVs is so high in the new initiates to injecting, which in turn leads to the high FOI estimates reported here? Is the infection due solely to injecting behaviour, or is it due to infection for some other reason? Background HBV infection where transmission occurs between IDUs and non-IDUs was incorporated in the FOI model and was found to be at very low levels, this suggests that the major cause of HBV infection in new initiates is due to their injecting behaviour.

A simple heterogeneous model describing the mixing of new initiates and experienced IDUs was applied to estimate the impact of HBV vaccination in prisons on transmission of HBV in the IDU population of England and Wales. Estimates of the vaccination coverage of the IDU population from the model of the HBV vaccination programme in prisons were applied along with the FOI estimated in Chapter 5. The base case model (that assumes that the vaccination coverage on prison reception is 5% in 2002, 10% in 2003 and then increases linearly up to 50% in 2006) predicts that the incidence of HBV in IDUs might be reduced by almost 75% in 12 years, and the HBV prevalence (IDUs ever infected by HBV) may be reduced

from approximately 15% in 2002 to 6% in 2015. Sensitivity analysis demonstrated that the FOI estimates had a significant impact on the results obtained from the model. This emphasised the importance of obtaining reliable FOI estimates for application in this setting. Further sensitivity analysis examining the proportional mixing assumption found that alternative assumptions describing the contact between new initiates and experienced IDUs had very little impact on the estimated number of acute cases of HBV in the IDU population.

The cost-effectiveness of a number of alternative HCV case-finding scenarios on reception into prisons in England and Wales was examined. It was found that identifying those individuals that have not received a past positive HCV test, and have ever injected illicit drugs is the most cost effective approach to case-finding on prison reception. This shows the importance of identifying those individuals with a history of injecting drug use, which is the biggest risk factor for HCV infection. Over time it was found that the case-finding scenarios all become less cost-effective this being due to the impact of previously screened individuals returning to prison that do not need re-screening and the time taken to identify these prisoners. Sensitivity analysis showed the importance of encouraging eligible prisoners to accept the offer of an ELISA test, with a reduction in uptake having a large impact on cost-effectiveness. This work is novel in that rather than applying a hypothetical model in which a set number of individuals are exposed to screening as a 'one-off', the impact of previously screened individuals returning to prison on the cost-effectiveness was considered.

### **8.3 Limitations of study and future research**

At the time when analysis of the characteristics of the IDU population was undertaken the UAPMP (section 1.2) had collected surveys on the IDU population up till 2001 and as such surveys up to this time were used in this analysis. Data from these surveys has continued to be collected and therefore the findings here, particularly the rates that IDUs start injecting drugs and leave the IDU population can be updated to represent more up to date information. This would then allow the model describing the flow of IDUs through prisons to be re-parameterised. Future work could apply this method of estimating the characteristics of the IDU population to other surveys as they become available particularly those that survey IDU populations outside England and Wales. This will provide further insight into the usefulness of this method of analysis, and will allow comparisons between alternative IDU populations to take place. However it is acknowledged that collecting annual surveys from current IDUs that is suitable for analysis such as this is a considerable undertaking.

During calculation of the rates that IDUs leave the IDU population it was not possible to distinguish the reason that injectors leave the IDU population although it is likely that this is due to a combination of cessation and perhaps death due to the chaotic life style associated with drug use e.g. overdose or bad health due to injecting related infection. For the calculation of the average injecting career length of IDUs and parameterisation of the flow of IDUs through prisons it was therefore assumed that the removal rate is the same as the stop rate, however by considering death rates obtained from other sources (Darke & Zador, 1996; Ghodse *et al.*, 1998; Hulse *et al.*, 1999; Law *et al.*, 2001), future work could consider what impact death has on the removal rates estimated here.

Throughout this thesis a current IDU has been defined as an individual that has injected in the previous 4 weeks or in the case of the flow of IDUs through prison defined as injecting within 4 weeks prior to reception into prison. However this simplistic approach to the complex behaviour of IDUs does not acknowledge that

many IDUs may stop drug using for extended periods of time before relapsing into their previous drug using behaviour. Cohort studies that follow IDUs and ex-IDUs for an extended period could provide a greater understanding of the rates that IDUs start and stop using drugs whether this be temporary or on a more permanent basis, although studies such as these would certainly be expensive and time consuming to implement.

Data from a survey of prisoners in 10 prisons was used to parameterise the model of the flow of IDUs and non-IDUs through prisons in England and Wales (Weild *et al.*, 2000), however only one of the surveyed prisons included females. As this was felt to be insufficient to extrapolate to represent the whole of the female prison population in England and Wales only males were considered in the analysis. For consistency the parameters describing the rates that IDUs start injecting and leave the IDU population were also parameterised from male IDUs. Data on the time spent in prison for each spell of imprisonment for males and females shows that females spend less time in prisons than males (Home Office, 2003). The faster that IDUs pass through prisons the quicker they will reappear on prison reception and this will increase the chance that they will participate in a prison reception based intervention. Therefore by only considering male IDUs in this analysis a conservative view of the potential of the prison interventions has been considered. However if data becomes available that can be extrapolated to represent the whole of the female prison population then the models here can be re-parameterised to reflect this.

The prison survey (Weild *et al.*, 2000) informed as to the proportion of the prison population that were current IDUs and the average length of time that IDUs spend incarcerated during a spell of imprisonment. However by using these data it must be assumed that the offending characteristics of IDUs have not changed since 1997. And while it is acknowledged that these data are old, no further surveys have been undertaken of sufficient size that would enable the model of the flow of IDUs through prison to be re-parameterised. However as more up to date data becomes available of sufficient quality to inform as to the current offending and re-offending characteristics of IDUs and non-IDUs within prison, then this model may be re-parameterised to reflect this. A further advantage of collecting more prison based

data is that multiple prison surveys would also allow time trends in the offending characteristics of IDUs to be investigated.

The model of the flow of IDUs through prisons in England and Wales describes a simplistic approach to the workings of the prison population as individuals enter, stay, and then exit prisons. The prison population in England and Wales is housed in 138 prisons of varying type, housing different types of prisoner depending on the prisoner's sex, length of sentence, or type of offence. During their time in prison, prisoners may be transferred between prisons for numerous reasons. The model of the flow of IDUs through prisons has not considered different types of prison, but instead models the whole of the prison population in England and Wales with variation in age and injecting status. One obstacle to incorporating prison transfers into a prison based model is that data on the rates that prisoners are transferred between prisons is very sparse and further to this if transfers between prisons are to be incorporated in the model then the issue of previously imprisoned individuals returning to prison by type and perhaps location would need to be considered.

The model of the flow of IDUs through prisons assumes that the IDU population of England and Wales is a closed population in that the migration of injectors into the population from other countries is not considered. These individuals could potentially bring infection into the population which is in addition to the transmission that is already occurring. If the rate at which infected injectors from other locations flow into the IDU population in England and Wales can be evaluated along with the prevalence of infection within this group, then the impact of this on the effectiveness of the HBV prison vaccination programme both on vaccination coverage and HBV transmission could be considered.

Apart from Chapter 7 that considered the cost-effectiveness of HCV case-finding on reception into prison, there has been very little consideration regarding costs in this thesis. The effectiveness of the HBV vaccination programme in prisons has been considered here in terms of the proportion of the IDU population that may be captured by vaccination, and its impact of prison vaccination on HBV transmission within the IDU population of England and Wales. A further measure of effectiveness

would be to estimate the cost-effectiveness of administering HBV vaccination in prisons. This would consider the cost of administering the programme and the potential benefits to the health care provider that would be made due to a reduction in the transmission of HBV and an increase in the quality of life of individuals that would otherwise have had HBV. Previous studies have considered the cost-effectiveness of HBV vaccination in a prison setting (Jacobs *et al.*, 2004; Pisu *et al.*, 2002) although this proposed future work would be novel as by applying models described here, this would allow the use of dynamic modelling with the FOI changing over time to be undertaken.

The HBV vaccination programme in prisons continues to expand in prisons across England and Wales and as of July 2006 111 out of the 143 prisons in England and Wales reported to the Prison HBV Vaccination Monitoring Programme at the HPA that they were offering vaccine to prisoners on reception into prison. At the time when this research was undertaken, the most up to date data informing the current state of the prison vaccination programme was used to inform the vaccination scenarios, e.g. data collected in 2003 described the proportion of individuals on reception into prisons receiving 1, 2, or 3 doses of vaccine. However it is acknowledged that the results here can certainly be updated to reflect new information as it becomes available, although a range of alternative vaccination scenarios have been considered here and new data is unlikely to change the conclusion that prison is a good place in which to vaccinate IDUs against HBV.

The FOI model proposed here relies heavily on data describing the injecting career length of current IDUs as this informs as to the length of time that an IDU is exposed to BBV infection. The injecting career length has been calculated for each IDU by considering the reported difference between IDUs current age and age at first injection. A possible improvement to this and to get an additional insight into the injecting career length of IDUs might be to actually ask how long an IDU has been injecting. To validate IDUs responses to surveyed questions, both this question and the questions relating to age at first injection and start age could be asked. The model has estimated that new initiates to injecting are at increased risk of BBV infection compared to more experienced IDUs although additional data on new initiates would



be beneficial to confirm the findings here. However as has been previously discussed the IDU population a hard-to-reach population, and finding new initiates to survey is inevitably problematic.

Although the model structure described here has allowed for the possibility of trends in the FOI over time no significant trends were detected by the model. However it has been shown in analysis from data from these UAPMP surveys that the prevalence of HCV in the IDU population of England and Wales has increased in recent years (section 1.3.1.2). As the data used in the FOI analysis only considered susceptibles to infection and FOI estimates were obtained simultaneously for both HBV and HCV infections, those IDUs that were vaccinated against HBV were excluded from the analysis. The impact of this is that many of the IDUs in the survey that are diagnosed as being HCV positive, will receive HBV vaccination and therefore be excluded from this analysis. Future work may consider each virus separately in an attempt to identify trends over time, although individual heterogeneity of risk behaviour could not then be considered.

The FOI for BBVs amongst IDUs is inevitably a product of many components that describe the injecting behaviour of IDUs. These components include but are not limited to the number of injections per unit time, the number of instances of sharing per unit time, and the proportion of reused needles that are adequately cleaned. It would be both informative and useful for future modelling work if the FOI estimates described here could be described in terms of the injecting behaviour of IDUs in England and Wales. This would be of particular benefit for future work that considers the impact of intervention measures that target IDUs behaviour on the prevalence and incidence of HCV or HBV within the IDU population of England and Wales.

As has been shown during the sensitivity analysis of the model of the HBV vaccination programme in prisons (Chapter 4) the estimated size of the IDU population has a large impact on the model results describing the proportion of the IDU population that may be vaccinated over time on reception into prisons in England and Wales. Data from a previous study has been used to estimate the

proportion of the prison population that is a current IDU (Weild *et al.*, 2000), therefore a larger estimated IDU population results in a smaller proportion of IDUs being exposed to vaccination on prison reception and this will inevitably have less of an impact on HBV transmission within the IDU population. Results obtained here based on an assumed IDU population size of 160,000 provide estimates of the number of acute cases and HBV prevalence within the IDU population that have been broadly validated by data which help to give confidence to the validity of the assumptions made here, however further work that can provide estimates of the size of this hard to reach population will always be of benefit.

The models proposed here have not considered BBV transmission in non-IDUs, whether this is transmission between IDUs and non-IDUs or in non-IDUs alone due to risk factors other than injecting (e.g. transfusion, blood product recipient, or sexual exposure as appropriate) to fully measure the impact of intervention measures that target BBVs in the IDU population the transmission of infection in non-IDUs should be incorporated. A reduction in the prevalence of BBVs within the IDU population may have an impact of reducing the prevalence in the non-IDU population. Although it is likely that due to the migration of individuals from countries of high BBV endemicity (HBV, HCV, or HIV) into England and Wales, the impact of prison interventions on the prevalence within non-IDUs will be reduced.

As discussed in the introduction (section 1.6) previous studies have considered the possibility of adopting an individual based model to describe the IDU population and the transmission of infection within it (Peterson *et al.*, 1990; Mather & Crofts, 1999; Kretzschmar & Wiessing, 1998; Atkinson, 1996). The HBV transmission model proposed here has considered a relatively simple model structure in which the contact between new initiates and experienced IDUs is described. A more complicated individual based model could perhaps be considered although due to the data requirements associated with a model of this type the parameterisation of the model may prove difficult. Assumptions regarding the transmission of HBV between individuals, how the individuals flow through prison, and their exposure to the prison vaccination programme on an individual basis would have to be made. It has been shown in Chapter 5 that there may be individual heterogeneity of risk behaviour

within the IDU population that is independent of injecting career length, although the model structure proposed here does not allow for this possibility. Future work may involve the modification of the model structure by assigning IDUs based on their injecting behaviour to be either high-risk or low-risk from BBVs that better represents the characteristics of the IDU population. This could include the number of injections, the number of partners, and may include the possibility of interaction between buddy and stranger users (Kretzschmar & Wiessing, 1998). However more complex models will rely on detailed data with which to parameterise them and this may not be readily available.

A consequence of taking the vaccination rates from the HBV vaccination programme in prisons and applying them to the HBV transmission model is that FOI is assumed to be constant both inside and outside prison. As has already been discussed (section 1.4) IDUs may be at increased risk of BBV infection in a prison setting due to the lack of availability of clean needles, although it is increasingly difficult to get an informed estimate of the FOI for BBVs that are dependent on location. If this were to be done it is proposed that a cohort study would have to be initiated that follow IDUs for a period of time which would involve frequent BBV testing as their imprisonment status changes. However it is likely that due to the length of time a study such as this would need to be implemented, the cost of following IDUs as they change location and the number of IDUs that would be required to get informed FOI estimates, this approach would be problematic, while there would also be ethical issues of having to monitor individuals as they become infected from BBVs without offering any intervention. Future work could consider assumptions regarding the increased risk of infection inside prisons and how these would impact on the transmission results estimated here, although offering vaccination on reception into prisons must have a positive impact on the FOI in the prison setting.

Only the cost-effectiveness of HCV case-finding in a prison setting has been considered here although it is acknowledged that the inclusion of the costs and benefits associated with treating individuals that have been identified with HCV in prison will play an important role in judging whether to implement an HCV case-finding programme on reception into prison. Previous studies have considered the

cost effectiveness of HCV treatment (Wright *et al.*, 2006; Stein *et al.*, 2002; Stein *et al.*, 2004) although there are issues regarding the treatment of individuals that are specific to a prison setting, e.g. the possibility that some individuals will follow a treatment pathway that involves continued treatment in the community following discharge from prison. The work here examines the best approach to identifying individuals that may be eligible for treatment and future work will consider the cost effectiveness of HCV treatment in a prison setting in England and Wales.

BBV infection is not the only problem that faces IDUs. It has been shown in previous studies that IDUs are at increased risk of mortality immediately following spell of imprisonment (Seaman *et al.*, 1998; Bird & Hutchinson, 2003), this frequently being due to increased drug taking following a period of abstinence. Future work could consider this problem by modifying the model of the flow of IDUs through prison as described in Chapter 3 to reflect this increased risk to IDUs. Following this a cost-effectiveness study could be undertaken to compare the cost of targeting IDUs on discharge from prison to reduce the mortality risk versus a do nothing scenario.

Issues that are of interest to the population outside prison do not stop being a problem once individuals enter prison. Over the last few years much research has been undertaken into severe acute respiratory syndrome (SARS) and pandemic flu in the general population both in England and Wales and around the world. The potential impact of these infections within the prison population could be investigated, although it is acknowledged that it would not be necessary to use a model stratified by IDU status in this case.

## **8.4 Concluding remarks**

This thesis has estimated the characteristics of the IDU population and its risk of infection from HBV and HCV and following this a range of alternative prison based intervention measures that target IDUs and their infection from BBVs have been considered. It has been shown that IDUs that start injecting at a younger age are likely to inject for longer than those individuals that start injecting later in life, while it has been shown that new initiates to injecting are at increased risk of HBV and HCV compared to more experienced IDUs. This is of importance as it provides strong evidence that younger IDUs with shorter injecting careers are particularly vulnerable and a special effort should be made to target intervention measures at this sub-group of the IDU population. A model that describes the flow of IDUs through prisons in England and Wales has been proposed and parameterisation of this model provides further evidence that IDUs are at increased risk of imprisonment and pass through prisons at a faster rate compared to non-IDUs. The impact of the HBV vaccination programme in prisons was estimated considering both the coverage of the IDU population with vaccination and its impact on HBV transmission within the IDU population. This showed that prison is a good location in which to target IDUs for HBV vaccination and that this may have a significant impact on the transmission of HBV within the IDU population. Finally the cost-effectiveness of HCV case-finding on reception into prisons was estimated showing the importance on the cost-effectiveness of targeting individuals that have previously injected illicit drugs and not received a positive HCV test in the past for testing. The work here demonstrates some of the applications of a fully parameterised model of the flow of the IDU population through prisons. However this model relies heavily on data sources that inform as to the rate that IDUs start and stop injecting and their offending characteristics. It is therefore important to the relevance of the results obtained from the model that data that reflects the current characteristics of the IDU population is available.

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